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PRENATAL RUBELLA

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This study has demonstrated that cultural and serological studies are necessary for the proper identification of rubella infection in the new born. In the future much diagnostic information must come from our virus laboratories. The morbidity of thi infection during prenatal lif is severe especially in those children exhibiting positive virus at birth. Th in idence f heari g loss in the Baltimore epidemic was high Virus infection in the inner ears of our t mporal bones resulted in changes of varying degrees within the cochlea duct and the saccule Damage to th ears f a child frequently results in differing degrees f deafness on the two sides. A preliminary report was made on this study in 1966 (Bordley *et al*)

Prenatal rubella was first recognized as a cause of congenital defects in the human offspring following the Australian rubella epidemic of 1939–1941 In 1941 Gregg described congenital cataracts in babies exposed to rubella during the first trimester of pregnancy and in 1943 Swan re ported deaf muti m in rubella babies of this same epidemic. Patent ductus arteriosus and other cardiovascular defects including pulmonic stenosis are now known to be part of the picture resulting from prenatal rubella Other defects described are microcephaly thrombocytopenia, mental retardation, failure of normal growth and lack of normal cell populations in arious organ

Two years after Swan s report on deaf-mutism, Carruthers (1945) published his observati ns on prenatal rubella. He found 116 children with severe deafness out of 147 births following prenatal infection where the infant had shown other injuries at birth. The same year 1945 he reported on the hi t logical changes following prenatal rubella. These changes were limited to the inner ear and were associated primarily with the cochlear duct and saccule Hi ob ervations were subsequently confirmed and elaborated upon by v Tondurry (1951) Schall *et al* (1951) Kamerbeek (1949) Nager (1952) Lindsay *et al* (1953) and their co-workers.

Up to the present time there has been very little correlation between virological or serological tudies and the morbidity of this disease as it

This study h been pported by National I stitutes of Health Grant N.B 03371 nd by the Subcomittee for H r g in Childre of the America Academy of Ophthalmolog nd Otol ryngology

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TABLE 2. *Rubella history v laboratory results*

Maternal history	Viral positive	Serology positive	Total
Clinical rubella	20	61	81 (49 %)
Subclinical rubella	10	74	84 (51)
Total			165

developed no clinical evidence of rubella although this group of 84 mothers gave birth to 10 children exhibiting positive virus cultures neonatally and 74 of the offspring had positive serology These findings would suggest a possible explanation for the etiology for the hearing loss in many children that in the past we have been unable to find the cause for their handicap

The hearing tests used in our study consist of two types the first, the screening test which is based on the Ewing Test Technique (Ewing & Ewing, 1944) the second the complete hearing evaluation which is carried out on all those children failing their screening tests. The latter evaluation employs the Ewing Test Techniques but in addition makes use of a special speech hearing evaluator which employs puretone frequency ranges between 50 and 10,000 hz, monitored human voice, white noise high pitched rattle sounds and squeaky toy sounds To pass the second test, the child must give consistent responses which should include efforts at localization. Such seeking for the sound source is done by the average child in the test environment at a sound level of 30 decibels s p l or even less. Failures in our study are recorded when there is no consistent response to sound at or above 50 decibels s.p.l Inconclusive results following this second series of tests are followed up by electrodermal audiometry and summated cortical potential studies on the children in question Using these methods to establish hearing loss, we have found that the virus positive group has a failure rate of 56.6% whereas the serology positive group has a failure rate of 41.5% (Table 3)

In the past, it has been generally believed that the danger of prenatal rubella infections lies in the first trimester In our study this has not been true One out of the three viral positive children following second trimester rubella showed a hearing loss, and seven out of ten children with a positive

TABLE 3 *Hearing test results* (165 cases)

	Passed	Failed
Viral positive (30)	13 (43.4%)	17 (56.6)
Serology positive (135)	79 (58.5)	56 (41.5)
Total	92 (55.6)	73 (44.4%)

relates to congenital defects In 1962 the rubella virus was isolated by Parkman *et al.*, and Weller & Neva (1962) The isolation of the virus was followed by the development of serological methods for identification of rubella by Alford *et al* (1964) and by Sever *et al* (1965) The rubella epidemic which occurred in the Baltimore area in the spring of 1963 and lasted through the spring of 1965 offered an excellent opportunity to apply these newly developed techniqeus for the study of the morbidity of the disease The studies reported in this paper were carried out at The Johns Hopkins Hospital using the facilities developed for the Collaborative Project on Cerebral Palsy under the direction of Hardy *et al* (1966) The virological and serological studies were done in the Perinatal Infectious Disease Laboratory at the National Institute of Neurological Diseases and Blindness under the direction of John Sever M D

The report is based on a group of 165 children whose prenatal exposure to rubella has been confirmed by laboratory studies and who have completed general medical reviews, neurological examinations and hearing studies Some interesting findings will be reported from the remaining group of rubella confirmed children who have not yet had the complete battery of examinations designed for this protocol This incompletely tested group numbers about 300 children The 165 completely studied children will be referred to as the "study group"

Confirmation of rubella in both groups was by (1) positive viral cultures from the child or (2) positive serological reactions obtained from the child and/or its mother The latter include antibody neutralization techniques, compliment fixation tests and/or hemoglutination inhibition studies This last test has proven particularly effective in the severely damaged children In the study group 30 of the children showed positive viral cultures and 135 gave serological positive tests (Table 1) One of the important facts demonstrated in these studies and in those of a number of other investigators (Baylor Rubella Study Group 1967) is that the rubella virus under the conditions found in fetal growth and early infancy survives a surprisingly long time Re-cultures showed a persistence of the virus in a number of the children for a period of from 4 to 8 months postdelivery One child had a persistently positive culture for 10 months

The value of laboratory investigation is particularly well demonstrated when one compares the clinical manifestations of rubella with the laboratory findings In our study group (Table 2) 49% of the mothers had a history of the clinical symptoms and signs of rubella during their pregnancy 51%

TABLE 1 *Cases in study*

Viral positive	30 (18%)
Serology positive	135 (82%)
Total	165

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Total	92 (55.6%)	73 (44.4%)

TABLE 4 *Summary of hearing test results v maternal history*

Maternal history	Hearing test Passed	Failed
1st trimester rubella	17 (32 %)	36 (68 %)
2nd trimester rubella	12 (60 %)	8 (40 %)
3rd trimester rubella	4 (50 %)	4 (50 %)
No positive rubella history	59 (70 %)	25 (30 %)

serology born following second trimester rubella showed hearing loss In our study group four children showed a positive serology following third trimester rubella and all four of these failed their hearing tests (Table 4) These findings point to the fact that rubella in the second and third trimester may also be teratogenic. Table 5 shows the hearing tests failures of the children and the trimester in which the mother was infected as well as the relationship of hearing loss to virus positive and sero-positive findings Further confirmation of fetal injury is found in the as yet incompletely studied group of children In this group there are 19 mothers with a history of second trimester illness (Table 6) In two of these there was fetal loss where cultures of the fetus showed live virus There were 12 live births where rubella was confirmed There were 2 live births where rubella was suspected, but no laboratory confirmation was obtained. In three mothers the illness was thought not to be rubella Of the 17 viable children from the 19 pregnancies 6 were abnormal 3 were suspect of some abnormality and 8 were normal

In our large incompletely tested group 2 children were born whose mothers had rubella previous to conception In the first case the mother had confirmed rubella 2 months before conception. Live virus was grown from the child, and he bore the stigma of the disease The second child whose mother had rubella one month before conception showed a positive serological reaction and had cardiac defects typical of the stigma of prenatal rubella

TABLE 5 *Maternal history v hearing test results*

Rubella history	Viral positive Hearing test Passed	Failed	Serology positive Hearing test Passed	Failed
1st trimester rubella	3	14	11	22
2nd trimester rubella	2	1	10	7
3rd trimester rubella			4	4
No history of clinical rubella	8	2	51	23


1


2


3


4


5


6

sound stimuli Virus was cultured from nearly all the body organs at autopsy and many congenital defects were identified at this time Carotid profusion was carried out immediately after death with 5% formalin The autopsy was performed within two hours of the time of death

Both ears in this case show a Scheibe-type change in the scala media and in the saccule The right ear appears to be the more serously involved, exhibiting a collapsed Reissner s membrane (Fig 1) The membrane seems to be adherent to the stria vascularis and is plastered against the organ of Corti The stria itself is smaller than normal and seems to be lacking the usual number of capillaries A number of sections show the tectorial mem brane to be rolled up and lying in the internal sulcus (Fig 2) There is what appears to be a single layered membrane covering the internal sulcus in several areas, and this membrane extends under Reissner s membrane The organ of Corti appears essentially normal The hair cells are plentiful and no changes were noted in the pillar cells In some areas some clear pink staining material was seen in the internal sulcus Nerve fibers and spiral ganglion cells appear plentiful There appears to be less change evident in the apical turn than elsewhere (Fig 3) The saccule shows changes that have been noted by a number of authors It appears partially collapsed A portion of the membrane appears adherent to the macula (Fig 4) There are a number of large epithelial cells that lie along this membrane near the point of adhesion These unusual cells appear in sec tions from both ears in this case (Fig 5) The remainder of the endo-lymphatic system including the utricle the semicircular canals and the endolymphatic sac is normal

The left ear is interesting because throughout much of its length Reiss ner s membrane is pulled away from the bony wall at its external attach ment rolling up the outer margin of the stria vascularis (Figs. 6 and 7) *This is particularly striking in the lower portion of the third turn of the* cochlea where the detachment has much the appearance of a cyst (Fig 8) The saccule of the left ear appears very similar to that of the right (Fig 9) No abnormalities were noted elsewhere in the endolymphatic system

The second pair of ears are from a 7 month fetus who lived only about 18 hours postdelivery No tests were done for hearing The mother had a rubella infection in the tenth week of pregnancy Positive cultures were obtained from the child at birth Only one ear the right shows any changes, and these appear rather minimal compared to those of the first case The cochlear duct is affected (Fig 10) Reissner s membrane is adh rent throughout most of its length to the organ of Corti There is some distor tion of the tectorial membrane under Reissner s membrane The organ of Corti appears essentially normal in both ears, and nerve fibers and spiral ganglion cells are plentiful In this case no changes were found in the stria vascularis The saccular membrane appears to be a little depressed (Fig 11) but is within normal limits The utricle semicircular canals and the lymphatic sac appear normal The left ear shows no changes (Fig 12)

DISCUSSION

In reviewing the case records of 165 children exhibiting positive laboratory evidence of prenatal rubella contracted during the Baltimore epidemic 1963–1965 a high percentage of hearing loss has been documented Those children from whom live virus could be cultured showed a higher percentage of damage than the children exhibiting only positive serological findings.

In this study it has been demonstrated that a high incidence of children suffering the stigma of prenatal rubella are born of mothers who have had subclinical rubella during their pregnancy Prenatal rubella may be teratogenic in the second and third trimester In two instances in our overall study rubella contracted in the preconception period appeared to be the cause of rubella deformed babies.

Children carrying live virus at birth act as test tubes in which the organism continues to live for many months Something occurring in the mechanism of pregnancy would seem to promote continued growth of the virus, and dissemination of the virus takes place from the newborn (Cooper & Krugman 1966) Rubella virus infection apparently deranges something in the cells which results in failure to reproduce Such changes produce many types of injury from microcephaly to mental retardation Studies by Naeye & Blanc (1965) demonstrate that cell populations are smaller in infants born with the rubella syndrome than in those of normal infants. Plotkin (Ingalls *et al* 1967) and his group have speculated that cells that have ceased to divide may continue to produce virus for months. His group has found virus in in vivo preparations for as long as 208 days.

The pathology observed in the 4 temporal bones obtained in our study show that changes occur in the cochlear duct and in the saccule The lesions do not necessarily involve the ears of a patient equally This would seem to explain the reason for the difference in degree of hearing loss in the two ears of children following prenatal rubella

Rubella in pregnancy can damage a child while giving very little evidence of its presence in the mother The child may not only be damaged but because of a lack of any clinical history of prenatal rubella may be a menace to the community unless careful laboratory studies are carried out to identify the disease It would be well to cite how costly these infections may be The following case history points out how dangerous such children may be. This child was born at 40 weeks gestation weighing 2310 grams. He had bilateral cataracts, congenital heart disease and a rash which was petechial and ecchymotic. He had hepatosplenomegaly thrombocytopenia, bronchopneumonia, recurrent diarrhea, failure to thrive and a profound hearing loss. The virus was isolated from the placenta of the mother and from the rectum the eye and the bone marrow of the child The bilateral cataracts and the congenital heart disease was successfully corrected by

surgery This child is presumed to have been the source of infection for 3 student nurses who in turn infected 4 other student nurses. The estimated hospital cost to date for this child is $5970

ZUSAMMENFASSUNG

Die Untersuchungsergebnisse von 165 Kindern werden mitgeteilt die während der Rubella Epidemie in Baltimore (1963–65) an praenataler Rubella erkrankt waren und bei denen die Diagnose mit Virus Kulturen und serologisch bestätigt worden ist Die Bedeutung des Virusnachweises ergibt sich aus der Tatsache dass 51% der Mütter keine klinischen Erscheinungen zeigten währenddem bei den Kindern die Laboratoriumsuntersuchungen positiv ausfielen Bei einer Anzahl von Kindern war das Virus noch viele Monate nach der Geburt nachweisbar was von anderer Seite bereits festgestellt worden ist Diese persistierenden Infektionen bedeuten wahrscheinlich ein nicht zu unterschätzendes Gesundheitsproblem. Säuglinge mit positivem Virusnachweis bei der Geburt wiesen eine hohe Morbidität während der Schwangerschaft auf Hörschaden wurden in 56 6% der Kinder fest gestellt Drei Kinder (100%) die in den letzten drei Schwangerschaftsmonaten an Rubella erkrankten wiesen einen Hörschaden auf Von zwei virus positiven Kindern wurden beide Felsenbeine histologisch untersucht Drei Felsenbeine zeigten Innenohrveränderungen vom Typus Scheibe mit Entwicklungsstörungen des Ductus Cochlearis. In zwei Felsenbeinen war auch der Sacculus verändert Über die fortlaufenden Untersuchungen wird später wieder berichtet werden

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COCHLEAR ROUND WINDOW RECORDED RESPONSES TO ACETYLCHOLINE AND CLICK STIMULATION FOLLOWING DECENTRALIZATION

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The round window recordings of cats are distorted in the same way by either sectioning of the fibers at the internal meatus or placing lidocaine or dibucaine at the same site. The cleft between N and N grossly recovers within two hours following the section procedure or the use of lidocaine. Dibucaine causes a persistent distortion for the two hours. Due to the lack of correlation of the procedures and the distortion it is doubtful that the distortion is due to the presence of an injury potential. It is postulated that the block of efferents may be contributing to the changes produced. Intra-arterial injections of acetylcholine (20 μg) are equally effective in depressing N in the innervated as well as in the decentralized cochlea.

One purpose of this investigation was to explore further the meaning of the electrical tracing obtained from the round window of the cochlea. This type of recording was initially done by Adrian (1931) and further extension of its interpretation was presented by Derbyshire & Davis (1935), Tasaki (1954), Davis (1957 and 1960) and Simmons & Beatty (1962). The nonneural component (microphonics, MC) represents the hair cell activity and, within limits, faithfully reproduces the polarity and frequency of the stimulus. The neural components of this recording, when a short duration click is the stimulus, are spike potentials (N_1 and N_2). These are interpreted as being due to firing of the auditory afferents at the level of the modiolus. They are not influenced by varying the polarity of the acoustic stimulus. The neural components are more profoundly affected by the presence of anoxia (Gisselsson 1954), temperature changes (Fernández & Alzate 1959), stimulation of the olivo-cochlear bundle (Desmedt & Monaco 1961) or the homolateral cochlear efferents (Rossi *et al.* 1964 and Fex 1965), and the administration of certain drugs (Daigneault & Brown 1966 and Amaro *et al.* 1966) than is the non neural component of the round window recorded cochlear response.

For future study of the pharmacological activity of various drugs on this

This study was performed under Grant NB-06261-02, National Institute of Neurological Diseases and Blindness, National Institutes of Health, U.S. Public Health Service.

system it is important to learn what the trace obtained represents. The work of Fisch & Ruben (1962) on sectioned eighth cranial nerves in cats pointed out interesting alterati ns of the round window recorded tracing produced by the sections. The alterations consisted of displacing the foot of N_1 and "a slow negative potential present in the components of the cochlear response We decided to investigate this alteration of the tracing further by utilizing local anesthesia to block the eighth cranial nerve In this manner it was possible to compare the effects of the acute change produced by section with that of a reversible drug induced block of conduc tion

The other purpose of this investigation stemmed from our interest in the postulate that acetylcholine may be playing a role in cochlear efferent transmission. Preliminary research (Daigneault & Brown, 1966) using cats, indicated that injection of acetylcholine into the vertebral artery of the acoustically stimulated side produces depression of the N_1 component of the round window recorded responses to click timuli It was demonstrated that these results were not being produced by either anoxia or middle ear muscle activation being produced by the drug However as no eighth nerve sectioned animals were included we could not determine whether acetyl ch line was acting directly on the cochlea or on some part of the central nervous system and thereby producing cochlear efferent stimulation. Hence the other purpose of this investigati n was to determine through decentralization of the cochlea, whether intra vertebrally administered acetyl ch line was producing the N depression by acting at the level of the cochlea or via the central nervou system

METHODS

Eighteen adult cats of either sex were anesthetized with an intraperit neal injection of Dial-Urethane (0 70 ml/kg) Then the trachea a femoral artery and the left subclavian artery were cannulated and the left ear prepared for recording from the round window A lateral surgical approach to the ound window was utilized and when the bulla was opened, a silver tipped, spring-loaded electrode was placed upon the round window mem brane and n indifferent electrode was placed on nearby bone These elec trodes were fed into a DP0B Grass CRO pre-amplifier the output of which was fed into one of the channel of a 564A Tektronix oscilloscope An S4 Grass stimulat r was used to initiate a short duration click (26 dB, re 1.0 Volt = 6.0 dB) in a TDH39 Telephonics earphone placed close to the animal left ear (The square wave producing the click was 0.0 msec in duration, 0.03 olts, and was repeated at a rate of 1 every 2 seconds.)

The cochlear response to this click stimulus consisted of an optimal N with no distortion of it being produced by th small MC. In addition, the stimulator was used to synchronize the oscilloscope with 1.2 msec delay Permanent records of the cochlear responses were obtained using a C4

Grass Kymograph camera photographing continuously during control or injection procedures An AC-3 Industrial Acoustics Co animal chamber was used to provide acoustic and electric shielding of the preparation

The surgical exposure of the left eighth cranial nerve was performed using a posterior craniotomy approach The cerebellum was partly removed by suction until the left eighth nerve and medulla were exposed After control acetylcholine and saline injections were made 0 05 ml of a local anesthetic, either 1% lidocaine (5 cats) or 0.5% dibucaine (5 cats) was injected into the dural sheath about the nerve at the point where it enters the internal auditory meatus The area was previously packed with cotton to absorb any volume of anesthetic which may have spilled out when the needle was withdrawn In the animals whose eighth nerves were sectioned (6 cats) the cut was made at approximately the same site with a wire loop in order to minimize damage to the arterial supply of the cochlea. In all exposures of the eighth cranial nerve a Bausch and Lomb dissecting microscope provided with a parallel light source was utilized for optimal visualization of the surgical field

Whenever it was necessary due to local anesthetic depression of the respiratory center the animal was placed on artificial respiration (this depression occurred in 2 cats)

Arterial pressure was measured from the femoral arterial cannula using a Statham arterial pressure gauge connected through an E&M physiograph

The drugs tested on the cochlear responses were administered via an arterial route using a three-way valve connected to PE 90 polyethylene tubing This was accomplished by way of a retrograde injection (i.e) made into the cannulated left subclavian artery (Tributaries of the subclavian outside of the thoracic wall were tied off so that most of the injected drug would be sent into the left vertebral artery) The drug injection was followed by a wash consisting of isotonic saline The total individual dose of acetylcholine iodide (ACh) administered was 18–25 micrograms in a volume of 0 08–0 12 ml Control saline injections were of the same volume The wash consisted of a volume of 0 80 ml saline

Statistical analyses were performed comparing all drug administrations before and after the blocking procedures as well as the effects of the various procedures on alteration of the tracing using a one-tailed unpaired Student t tests (Dixon & Massey 1957) The level of significance accepted in all of these tests was $p < 0\ 05$

RESULTS

The data of the animals recordings before and after the local anesthetic application and eighth nerve section are reported in Table 1 During the 1 to 2 hour period after either section or local anesthetic application the amplitude of N_1 gradually decreased The procedures of applying the local anesthetics as well as that of the surgical section distorted the neural

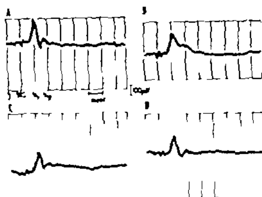


Fig. 1. The sequence of [illegible]. (A) control, (B) 10 min after section of the eighth cranial nerve. (C) 30 min subsequent to the section. (D) 3 hrs following the nerve section. MC, microphonics; N_1 first spike potential; N_2 second spike potential.

portion of the round window recorded cochlear response by reversing the cleft between N_1 and N_2 (see Fig. 1 B). Considerable recovery occurred with both the lidocaine treatment and surgical section inside of two hours. With the long-acting local anesthetic, dibucaine, considerably less recovery occurred in two hours. Upon subsequent sectioning of two of the five animals after their recovery from the lidocaine treatment, the usual *pattern* of distortion did occur.

The i.a. injection of ACh produced a *significant depression of the* N_1 as is shown in *Table 1*. These injections did not produce a measurable change in either direction, of the MC. ACh was as active in producing N_1 depression after the block or section as it was before those procedures. Subsequent to the recovery from the shorter duration local anesthetic, lidocaine i.a. ACh was as effective as before or during the local block.

DISCUSSION

The inhibition of nerve conduction at the space between the internal auditory meatus and the root of the eighth cranial *nerve, by either* section or local anesthesia, initially produces the same *distortion of* the round window recording. This distortion is mainly associated with the cleft between N_1 and N_2 (Fig. 1). In these series of experiments *we did not observe* a consistant initial alteration of the amplitude of *MC or of* N_1. This negative finding on MC seems to conflict with the findings of Rossi *et al.* (1964), however the parameters of stimulation that we used were not of the type necessary for optimal study of small *changes* in MC, as were those used by Rossi *et al.*

The cleft alterations did follow a *definite pattern* of recovery in each specific series of experiments, as can be seen in *Fig.* 1 and Table 1. The

TABLE 1 *The response produced by section or local anesthetic of the 8th cranial nerve of the anesthetized cat (dial urethane)*

±S.E.M. = Standard error of the means.

Procedure	Nerve section		Lidocaine		Dibucaine	
No of cats used	8		5		5	
	Before	After	Before	After	Before	After
μV[a] cleft alteration						
±S.E.M. (min)						
0	−121±11		−101±37[c]		−138±19[c]	
5–10		+134±21		+80±27		+1 5±26
30–60		+ 20±15		+ 8±22		+116±17
90–120		− 34±14		−59±10		+ 78±13[d]
μV[a] N amplitude						
±S.E.M (min)						
0	343±42		514±23		421±49	
90–120		251±22		309± 3		306±30
% N maximum depression						
±S.E.M (min)						
Produced by						
20–25 μg ACh Br i.a.						
0	22± 4		27± 7		21± 8	
90–120		23± 2		27± 4[b]		18± 3[b]

[a] The μV values are preceded by (−) when the value is below the baseline and a (+) when the value is above the baseline

[b] $p > 0.05$ no significant difference was obtained when compared with the Before control

[c] $p > 0.05$, no significant difference when compared to the three groups zero time

[d] $p < 0.05$, significant difference was found when compared with the extent of recovery at the 90–120 min interval

sectioned nerve preparations showed considerable recovery even in one hour and in two hours the tracing had grossly recovered since by this time a cleft was demonstrable between N_1 and N_2. This recovery raises a question concerning Ruben's postulate that the injury potential produced by the section may be responsible for the alteration Since the inflicted injury is permanent and the tendency toward recovery occurs within the first hour the injury per se must not be the primary cause for this effect Any further recovery two hours after the section progresses much slower (Fisch & Ruben 1962) and was not studied by us

The distortion produced by the local anesthetics differed only in the pattern of recovery observed In these series, no extensive injury potentials were produced therefore indicating that injury of the eighth nerve does not correlate with the observed alteration During the two hour observation period the dibucaine treated nerves did not recover any appreciable amount while the lidocaine ones did This is much in agreement with the expected

duration of action of lidocaine as compared to dibucaine Thus it seems that the duration of effect of these two agents on the cleft distortion correlates well with their action of stabilization of the efferent and afferent nerve fibers of the eighth cranial nerve

Although no satisfactory explanation can be brought forward to explain the recovery of the tracing after eighth nerve section, the fact that both section and local anesthetic blockade produce similar initial distortions point to a common mechanism by which these dissimilar procedures produce their initial effects.

Since N and N_2 represent a unipolar volume conductor recording of auditory afferent activity (Davis, 1957) production of the cleft alteration between N_1 and N is probably due to a change in the eighth nerve afferent firing patterns.

The experiments which will pinpoint what role if any the efferent have in the production of this cleft alteration are that of either sectioning the fiber tract of the homolateral and/or contralateral cochlear efferents at the level of the medulla, as reported by Rossi *et al* (1964) or placing electrolytic lesions in these structures. Such experiments are in the process of being prepared.

The action of ACh in all of these preparations was consistent N was depressed by i.a. ACh whether the cochlea was innervated by the central nervous system or decentralized In none of these experiments did i.a. ACh produce a significant alteration of MC. This negative finding may be attributed primarily to the experimental design being inadequate for the detection of small changes in MC. Even so this data is at odds to that reported by Tanaka & Katsuki (1966) Their results indicate a consistent, substantial reduction in MC occurs after iontophoretic application of ACh into the cochlea and also indicate that much less depression of N occurs than of MC. The difference of routes of administration could be used to hypothesize the cause of the different results obtained By the iontophoretic route the drug would be offered to the Organ of Corti from the region of the hair cells while by the arterial rout it would be from the basilar membrane Since diffusion of ACh in an area rich in acetylcholinesterase would not be extensive it is possible that the drug did not diffuse into common areas. The results of Tanaka and Katsuki experiments still cast doubt on ACh having a role in efferent cochlear transmission since the stimulation of the contralateral efferent cochlear tract increases MC (Desmedt & Monaco, 1961 and Fex, 1962) Further investigations are needed to answer the question of the importance of acetylcholine's activity in the cochlea

ZUSAMMENFASSUNG

In Untersuchungen an Katzen wird gezeigt, dass Durchtrennen des Hörnerven am Eintritt in d Meatus custicus internus und Injektion von Lidocain (Xylocain) oder Dibucain an der gleichen Stelle im wesentlichen gleichartige

Veränderungen in den vom runden Fenster abgeleiteten Potentialen zur Folge haben. Im Falle der Durchtrennung des Nerven und ebenso bei Gabe von Lidocain zeigt sich nach Ablauf von 2 Stunden weitgehend wieder der ursprüngliche Einschnitt zwischen N und N_2, während die durch Dibucain ausgelöste Veränderung nach 2 Stunden noch im wesentlichen fortbesteht. Da somit keine Korrelation zwischen den Prozeduren und den Veränderungen vorliegt, scheint es nicht wahrscheinlich, dass die festgestellten Veränderungen auf einem Verletzungs-Potential beruhen. Es ist eher zu vermuten, dass eine Blockierung von *efferenten Bahnen zu den gefundenen Veränderungen beiträgt*. Intra-arterielle Injektionen von 20 μg Acetylcholin hatten sowohl bei innervierter wie bei dezentralisierter Cochlea den gleichen Effekt in der Senkung von N.

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PRESBYACUSIS

A Histological-histochemical Study of the Human Cochlea

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The cochleas of thirty aged people were studied histologically as well as histochemically to demonstrate the pathology of sensori-neural element in the organ of Corti. Loss of sensory cells was found to be most severe near the basal end of the cochlea. Nerve fibers, both afferent and efferent showed marked changes near the basal end and less towards the apex. These changes consisted of mixing and various processes of degeneration of nerve fibers. Changes of sensori-neural element seen from the apex to the basal end were indicative of a process of degeneration of the individual element.

Degenerative changes of the sensori-neural element of the human cochlea start as early as the second or third decade of life and continue to progress with aging, resulting in slowly progressive hearing loss—presbyacusis. It is also well known that the changes are not restricted to the organ of Corti and nerve fibers in the cochlea. Recently atrophy of the stria vascularis was found to cause a type of sensori-neural deafness (Schuknecht & Igarashi, 1964). Atrophy and loss of the ganglion cells have been observed in the cochlear nuclei as well as in higher auditory centers (Saxén, 1952; Schuknecht, 1955; Kirikae *et al.* 1964; Hansen & Reske-Nielsen, 1965).

As far as the cochlear sensori-neural changes are concerned they gradually proceed apicalwards from the basal end. Therefore when the cochlea is observed continuously from the basal end apicalwards, changes observed have twofold meaning: (1) Range of the degenerative process in the cochlea at the same time, (2) changes from the basal end to the apex might be a process of degeneration of the individual sensori-neural element as time goes by.

The present study was intended to show how the nerve fiber degenerated within the osseous spiral lamina as well as in the organ of Corti, using histological and histochemical techniques.

MATERIAL AND METHOD

The temporal bones of thirty aged people were studied in this work. Human cochleas were dissected after decalcification with 5 per cent solution

of trichloroacetic acid then Holmes silver impregnation method was applied The recipe and staining steps were described in detail in a previous paper (Nomura & Kirikae 1967) For the demonstration of acetylcholinesterase (AChE) in the efferent fiber Karnovsky s thiocholine method was used (Karnovsky & Roots 1964) The cochlea was dissected into pieces *without decalcification and incubated in the following solution*

0 1 *M* sodium citrate	0.5 ml
30 m*M* copper sulphate	1 ml
Distilled water	1 ml
5 m*M* potassium ferricyanide	1 ml
0 1 *M* phosphate buffer pH 6 0	6 5 ml
Acetylthiocholine iodide	5 mg

The reaction deposit is copper ferrocyanide It is brown in the tissue where AChE is present

After the incubation is completed the tissue is dehydrated in graded alcohol cleared in xylene and mounted with biolcit

RESULTS

Loss of nerve fibers in the organ of Corti was seen most prominently near the basal end Single nerve fibers were observed to end midway in the organ of Corti where sensory cells were missing The fibers were apparently in the process of degeneration Stumps of degenerating nerve fibers ended making an oval appearance (Fig 1)

The inner spiral bundle was coming into view in the same specimen when observations continued apicalwards. In this area no tunnel fibers and outer spiral bundles were present The organ of Corti was severely degenerated or missing

The outer spiral bundle appeared as a single fiber in the first row then *gradually adding fibers, it finally formed the normal three rows (Figs* 2 and 3)

Near the apical end the number of nerve fibers in the outer spiral bundle decreased Three rows of the bundles in most parts of the cochlea decreased to two or one at a light microscopic *level* This was not a loss of nerve fibers by degeneration but a normal morphology of the apical end (Fig 4)

The pathology of the sensory cells in the organ of Corti was severe near the basal end and less towards the apex, as with those of the nerve fiber

The outer hair cells were irregularly missing When seen from above downwards, the outer hair cells were seen slanting their tops toward the basal end However some of the outer hair cells were occasionally seen as slanting to the opposite direction suggesting missing, or disarrangement of supporting cells

Fig. 1. A degenerati g nerv fiber nea the basal end (8 mm area) N rv fibers re complet l missi g xcept thi one *OC*, Orga of Corti; *SL*, piral lamina. Holmes tain.

Fig. 3. Normal fiber distribution in th orga of Corti. Medial fibers re crossi g the tunnel slanting t the pical turn (t the right i this photograph). Basilar fibers re t king the ppos t direction. *OSB*, Oute piral b ndle; *T* t nel f Corti; *SL*, spiral lamina. Holmes stain.

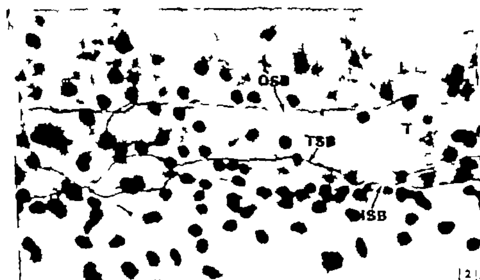


Fig. 2. Spiral f ber the organ of Corti. Only 1 row of the outer spiral bundle is present in the organ f Corti. *OSB*, Outer spiral bundle; *TSB* tunnel spiral bundl *T* t nel of Corti *ISB*, inner piral bundl Holmes stain.

FIG 4 N rve fibers in the api al turn of tl e human ocl l a *a* Out r hair cell *b* Inn h l cell habenul perf rata *d* api l nd h ll tre a H lmes stain

FIG H gl pow i w f the tu l f be d t piral l dles, Bulgi g, pos ibl ggreg tl f m toch d l th t n l fibe *OSB* O ter piral b dl H lmes t in

FIG 6 V ri o t f t l f be (m) Neurofibril re quit loosel rra ged l th icos t *1 2* and *3* lu t th f rst, eco d nd third row f ter piral *T* Tu l f Cort H lm st

FIG. 7 Efferent fibers in the spiral lamina and organ of Corti. Only 3 fibers remained in this area. Apparently no afferent fiber in the region. Organ of Corti is perfectly missing. OC, Organ of Corti; SL, spiral lamina. Phase-contrast. 1 mm area. AChE stain.

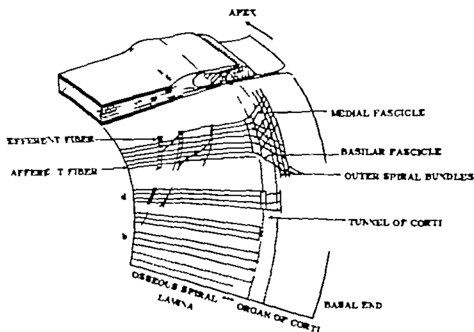


FIG. 8. Presbyacusis. Pathology of nerve fibers seen in the basal turn of the human cochlea. a, Loss of nerve fibers; b degenerating nerve fibers; d, partly missing nerve fibers; normal arrangement of nerve fibers.

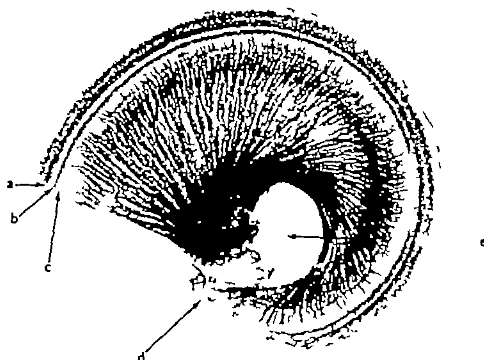
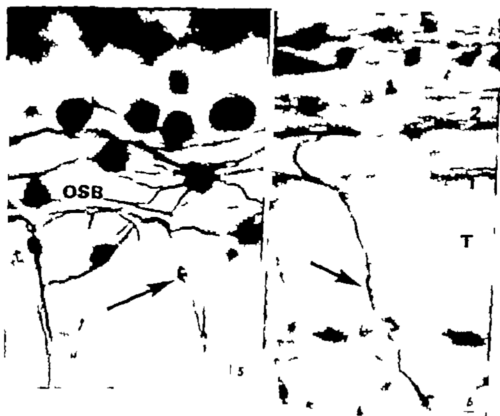


Fig. 4 Nerv fibers in the apical turn f th human coclle a, O t hal cell b I r hair c ll c habenula perf rata d pl l end e h licotrema H lmes st in



F 5 H gl pow l f ll t l f be d t l b dles H lgl g po ll ggreg tl f m t ch l th t l f be OSB Out piral b ndl H lmes t in

Fig. 6 Variet ty of t l f bu r m N rof b ll re q lt loosel rra ged l th ricos t 1 2 a d 3 de l th t t rs nd nd third row of t piral l dles T Tun l f Corti H lm t n

Karnovsky's thiocholine method for the demonstration of AChE was found to be excellent in histochemistry of the inner ear at electronmicroscopic level (Uchizono *et al* 1967)

A reaction deposit was observed attached to the axolemma of cochlear efferent fibers.

The axoplasma and myelin sheath were absolutely free from the enzyme activity The role of AChE in the efferent fiber is still unknown Electrophysiological studies have so far not proved that the efferent fiber is cholinergic (Desmedt & La Grutta, 1963 Katsuki *et al* 1965 Tanaka & Katsuki 1966 Fex, 1966)

It has been demonstrated that in the apical turn AChE activity is found to be weak in the outer hair cell area of animals (Wersäll *et al* 1961 Hilding & Wersäll, 1962) as well as in human cochleas (Nomura & Schuknecht, 1965 Nomura & Kirikae 1967) The present study of the human cochlea showed total nerve fibers, not only the efferent fiber were decreased in the apical turn

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ZUSAMMENFASSUNG

Die menschlichen Schnecken bei alten Leut n w rd n histologisch und histochemisch untersucht, um die path logischen Veränderungen im Cortischen Organ bei Altersschwerhörigkeit festzustellen Die herausführenden Nervenfasern wurden anhand der Karnovskyschen Methode fü di Lokalisierung mittels Acetylcholinesterase-Akti ität gefarbt. Da Verschwinden und di Degeneration de Ner enfasern waren sow hl an den herausführenden als auch an den zuführenden F sern i der Basalwindung am stä ksten und allmählich schwächer i der Richtung zur Apikalwi dung zu bemerken E ist anzunehmen dass die verschiedenen pathologischen Stadien die von der Apikalwindung n ch der Basalwi dung beobachtet wurden, den Degeneratio prozess der einzelnen Nervenfasern zeigen.

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Nerve fibers showed various morphological features en route to their destinations These were best seen in the tunnel of Corti where scarcity of the cellular elements gave us a good view of the nerve fibers. A spherical or spindle shaped swelling in the nerve fiber was frequently observed (Fig 5) Varicosity of the nerve fibers was also observed (Fig 6)

The efferent nerve fibers were decreased within the osseous spiral lamina as well as in the organ of Corti Degeneration and absence of nerve fibers were most severe near the basal end (Fig 7) When specimens were observed through a phase contract microscope the efferent and afferent fibers were clearly distinguished

Both afferent and efferent nerve fibers were in the process of degeneration in the cochlea of presbyacusis

DISCUSSION

Degenerative changes of the sensori neural elements were found to be severe in the basal turn of the cochlea as was generally accepted Changes were gradually less apicalwards Successive changes from the basal end apicalwards is possibly a degenerative process of individual elements as time goes by

The present study showed that both the organ of Corti and nerve fibers were missing and degenerating It was impossible to know which was the first to be affected sensory cells or nerve fibers As far as nerve fibers were concerned both afferent and efferent fibers were decreased In this respect Schuknecht (1955) had already stated that both afferent and efferent fibers degenerate in the epithelial type of presbyacusis Loss of the efferent fibers in the cochlea might be due to degeneration of the superior olivary complex where the cell body of the efferent fiber is located however it is also probable that the nerve fiber is going to degenerate secondary when its destination then sensory cells or afferent fibers, has been lost for considerable length of time

Bulging of the nerve fiber often seen in the tunnel is possibly aggregation of mitochondrion, because activity of the oxidative enzyme was demonstrated in the similar structure of animals It has been reported that in the tissue culture of the nerve cell a round particle was found moving in the living axon This phenomenon is called axoplasmic streaming This is another possibility of what the bulging in the nerve fiber is, but extremely difficult to prove

Varicosity of the nerve fiber seemed to be different from the structure just mentioned The fiber gradually widened into a spindle structure in which neurofibrils were quite loosely arranged Ramon Y Cajal (1959) described varicosity of nerve fibers as being found in the process of Wallerian degeneration of the sciatic nerve The present finding in the cochlea seemed quite similar and might indicate a degeneration process of the nerve fibers

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MECHANISM OF THE LATEROBASAL FRACTURES

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Thirty temporal bones of cadaver's skulls after fatal head injuries have been investigated. During explorations it has been ascertained that the transverse fractures of the pyramid involving the middle ear wall did not damage the ossicular chain, whereas the longitudinal fractures of the pyramid involving the middle ear walls are as a rule associated with the ossicular chain damage. The cases of the ossicular chain defect without any fracture of the pyramid were not rare. On the basis of the knowledge gained in experimentally induced fractures of the pyramid under different physical circumstances these facts are accounted for as a result of the differences in the solidity of the wall of the pyramid and in the mechanism of these fractures. In the longitudinal direction the pyramid is fractured by the mechanism of slide, while in the transverse direction the pyramid is fractured by the mechanism of drawing. The dislocation of the ossicles in the skull fractures not involving the pyramid is explained as a result of the various differences between the kinetic energy of the ossicular chain and the pyramid after the fall to the pad and as a result of the interference of the deformation waves, spreading within the bones of the pyramid and ossicular chain after the fall of the skull.

Many authors have recently reported cases of disruption of the ossicular chain due to head injury with or without fractures of the pyramid and the papers of many of them witness that the traumatic cause of the ossicular chain defects is not as rare as is often considered (Andersen *et al.* 1962, Ballantyne, 1966, Chvojka & Stroký 1962, Escher 1948, Filsberg & Filsberg, 1960, Gisselsson 1958, Hough, 1959, Kley 1966, Klos, 1957, Sadé 1964, Scott, 1964, Thorburn, 1957). Whereas in the transverse fractures of the pyramid the ossicular chain is usually spared, the longitudinal fractures of the pyramid frequently involve the conductive apparatus (Aubry & Pialoux, 1957, Fredrickson *et al.*, 1963, Gurdjian & Lissner 1946, Majer 1947, Proctor *et al.*, 1956). This fact is commonly explained by the location of the fracture line. Whereas the transverse fracture line usually penetrates into the internal acoustic meatus with severe injury to the labyrinth, avoiding the middle ear, the longitudinal fracture line courses through the roof of the middle ear cavity and the ossicles are often injured. We have studied changes in the ossicular chain due to head injury by exploring the temporal

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FIG. 2. Dislocation f the incudomallear joint due t longitudinal fract re of the pyramid.

where E = kinetic energy in Joule (kg m² sec⁻)
m = mass of the weight in kg,
v = velocity of the weight in m/sec,
g = gravidity acceleration 9.81 m/sec²
h = height in m from which the pyramid was fractured,

values of the kinetic energy necessary to produce th fracture of the pyramid were obtained The longitudinal fracture due to a blow on the upper wall was carried out fou times. The average value of the energy necessary to produce that fracture was 5.59 Joule.

2. The transverse fracture of the pyramid was produced in the same manner by a blow on it back wall The average value of the energy necessary to produce the fract re in 4 cases was 6 48 Joule

3 A blow was then produced in the same way on the upper wall of the pyramid which was fixed on its anterior edge of the upper wall on the portion of the bone of the greater wing of the sphenoid to be left *in situ* and on the foot f the back wall. The posterior edge of the upper wall and the whole ba k wall of the pyramid were free. Th distance from which the fracture of th pyramid was produced was recorded and, incorporating it in the same formula, we have gained the average value of the energy necessary t produce the f acture in 4 cases 4 72 Joule.

4 Blows on the upper wall of the pyramid were made by the same



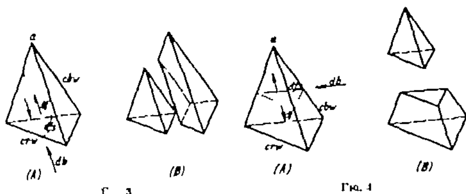
Fig 1 Dislocati n f th incud stapedial joint due to head injury without fracture of the pyramid

bones of the cadaver s skull after fatal head injuries and examined the middle ear structures either directly if the dislocation of the fragments was sufficient to appreciate the changes of the ossicular chain or endomeatally having removed a small piece of bone from the posterior superior bony canal wall to view the ossicular chain but avoiding the arteficial damage of the chain by greater manipulation In some cases we explored the middle ear after decalcification of the pyramid We have examined 30 temporal bones We have ascertained that the damage of the sound-conducting system without lesion of the pyramid is relatively frequent (of 18 cases there were 9 cases of ossicular chain defect) and that the transverse fracture of the pyramid coursing through the middle ear cavity walls does not cause the lesion of the chain (of 4 such transverse fractures there was only one case of ossicular chain defect whereas of 6 longitudinal fractures of the pyramid, directing into the same region there were 5 cases of the ossicular chain defect) This fact can be hardly explained by the location of the fracture line Trying to elucidate its causes and to verify some physical properties of the pyramid which are supposed to play an important role in the traumatic damage of the sound-conducting apparatus, we have carried out a series of measurements

METHOD

1 The petrous portion of cadaver s temporal bones was fixed to a pad and a blow was produced with the weight of 2 kg from the growing height The distances from which the fracture of the petrosa was made were recorded and incorporating them into the formula

$$E = 1/2\, m\, v^2 \quad v = \sqrt{2\, g\, h}$$



F 3 Fig. 4

Fig. 3. Mechanism of longitudinal fract es of the pyramid. (A) Directio of blow; B) dislocation of fragment by the mecha i m f sl d Apex of the pyramid; bw, cerebellar w ll f the pyramid rw cerebral w ll f the pyramid; db direction of blow; df directio of f rces; dfs, direction f fract re rface

Fig. 4 Mechanism of transverse fract res of the pyramid. (A) Direction of bl w B dislocation of fragment by the mechanism f drawing. Ape of the pyramid; cbw, cerebella w ll of th pyramid; crw cerebral w ll of the pyramid db direction f blow df direction f forces df direction of fracture surface

ing in the anteroposterio directi n Because the buttresses of the pyramid are not in equilibrium (on the anterior edge of the upper pyramid wall there is the greater wing of the sphenoid but the cerebellar wall is free without any buttress) the cleavage of the pyramid by drawing is replaced by the mechanism of slide This mechani m is analogous to that known in the physics f solid materials. Because of the thinness of the roof of the tympanic cavity (tegmen tympani) and the absence of a part f the external wall (tympanic membrane) the force e tend longitudinally to the pyramid more easily than in th transverse directi n The pyramid in the temporo-parietal di ection is directly exposed to injury and from th physical point of view the mechanism of slide is ea ler than the mechanism of drawing Th f rce necessary to fracture the pyramid is directly proportionate to its solidity and pr file Th solidity of the body in drawing is twice that in slide The force necessary to fractu e the pyramid by the mechanism of drawing i twice th f rce necessary to fracture the pyramid by the mech ani m of slid

When knocking th occipital area, in which the squama is thicker and the curv t re of th skull greate than in the temporal area, the impact is les widespread and the skull is m re resistant. Thi impact is further weakened by the penetration through th bones of the base f the skull and the extension to the foramen occipital m gnum which acts a an area of stress concentration This weakened force tries to sp lit the pyramid by the mechanism of drawing. Since the pyramid i more resi t nt to the mech anism of drawing than to the mech ni m of slide and the posterior wall f the pyramid is thicker than th external nd upper ones being strength-

weights (2 kg) and from the same heights (35 mm) The specimens were chosen in such a manner that in 4 experiments the pyramids had been fractured and in 4 cases they had resisted The surfaces of the pyramids were varnished with lacquer and the effect of the blow on the walls of the pyramid in these two different conditions was evaluated by the degree of *the peel-off of the lacquer* If the pyramid was fractured the lacquer around the fracture line was intact whereas in cases of non fractured pyramids irregular areas of the lacquer were peeled off

RESULTS

The results of our experiments are as follows

1 There is a difference in the solidity of the walls of the pyramid The back wall is more resistant to force than the upper one (see experiments 1 and 2)

2 The longitudinal fracture of the pyramid produced by the mechanism of slide, i e in circumstances in which the pyramid has no symmetrical strut in adjacent bones of the base of the skull (in experiment 3 we wanted to create a model picture of conditions of the normal human skull) can be made by less energy than the transverse fracture of the pyramid produced by the mechanism of drawing which is usual in this type of fracture (see experiments 2 and 3)

3 If the pyramid is fractured by the fall to the pad the small part of its kinetic energy changes into the deformation energy and the remaining greater part is spent in producing this fracture If the pyramid remains intact the whole kinetic energy of the pyramid changes into the deformation energy which produces greater deformation of its walls and ossicles (see experiment 4)

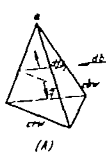
DISCUSSION

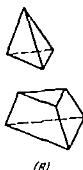
Our hypothesis as to what may have happened to cause the disruption of the ossicular chain during the head trauma is as follows knocking the temporoparietal area and producing the vertical fracture lines of the temporal squama which extend toward the base of the skull and thence along the anterior aspect of the petrosa toward its top causes a very widespread impact The impact is less widespread when knocking the occipital area and producing the vertical fracture lines of the occipital squama which extend to the foramen magnum and to the petrosa producing the transverse fracture *of the pyramid and sometimes the transverse fracture of the tym*panic cavity walls Because of the greater weakness of the temporal squama and the smaller curvature of the circumference of that region the skull is more vulnerable in this site The force applied in this area penetrates the pyramid easily longitudinally trying to split it by the mechanism of draw





I io. 3.





Fro. 4

Fig. 3. Mechanism of longit dinal fract res f the pyramid. (A) Direction f blow; B) dislocation of fragment by th mecha ism f lid a Apex of the pyramid; *cbw*, cerebell ll of the pyramid; *crw*, cerebral w ll f the pyram d; *db* direction f blo *df* directi of forces; *df* direction of fract re surface

Fig. 4 Mechanism f tra erse fract res of the pyramid. (A) Direction f blow (B dislocation of fragment by the mecha ism f drawi g Apex of the pyramid; *cbw* cerebella ll of the pyramid; *crw* cerebral w ll f the pyramid; *db* directio of blow *df* d rection of forces *df* d rectio of fract re surface

ing in the anteroposterior directi n Because the buttresses of the pyramid are not in equilibrium (on the anterior edge of the upper pyramid wall there is the greater wing of the sphenoid but the cerebellar wall is free with ut any buttress) the cleavage of the pyramid by drawing is replaced by the mechani m of slide This mechani m i an logous to that known in the physics of solid materials. Because f the thinness of the roof of the tympanic ca ity (tegmen tympani) and the absence of a part f the external wall (tympanic membrane) the force extends longitudinally to the pyramid m e easily than in the transverse direction The pyramid in the temporo-parietal direction i directly exposed to injury nd from the physical point of iew the mechanism of slid i ea ier than the mechanism of drawing. The f rce necessary t fr ctu e the pyramid is directly proportionate to its solidity and profil The solidity of the body in drawing is twice that in slide The force necessary to f acture the pyramid b y th mechanism of drawing is twice the force necessary to fracture th pyramid by the mech anism f slide

When knocking th occipital area, in whi h the squama i thicker and the curvature f the skull greater than in th temporal area, the impact i less widespread and th skull is m re resist nt This impact is further weakened by the penetr tion through the bones of the base of the skull and the extension to th foramen occipital m gnum which act as an area of stres concentration. This weakened force tries to split th pyramid by the mechanism of drawing. Since the pyramid is m re resi tant t the mech anism f drawing than t the mechanism of slide and the posterior wall of the pyramid i thicker than the external and upper ones, being strength-

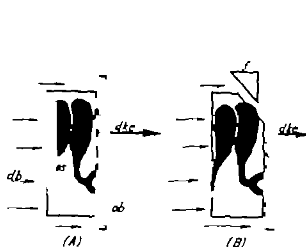


Fig 5

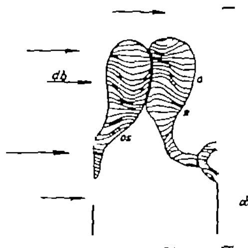


Fig 6

Fig 5 Ki etic nergy of the ossicles due to a blow of the pyramid on th obsta le (A) Int ct pyramid (B) fractured pyramid. *db* Direction f blow *dke* differenc between kinetic en rgy of the ossicl s and th pyramid *f* fragment f the fracture *ob* obstacl *os* ossicle

Fig 6 Interference of the deformati n waves travelling thro gh the i les. *a* Anti ode *db* directi n f blow *n* ode *ob* obstacle *os* ossicle

ened by the cellular system of the mastoid process, the pyramid in this direction is firm and safely protects the ossicles. The blow directed through the occipital area to the tympanic cavity does not disrupt the ossicular chain unless produced by excessively strong energy These facts explain the differences between our autopsy findings on the ossicular chain within longitudinal and transverse fractures of the tympanic cavity walls. The main factor in deciding whether the transverse fracture of the pyramid is associated with the damage of the ossicular chain or not is the energy by which the impact is carried out and the mechanism of fracture—not its location

In several circumstances (excessive blow and solid walls of the pyramid) the ossicular chain may be disrupted without any fracture of the pyramid the blow being applied to the temporoparietal area In 8 cases of damage to the ossicular chain with intact pyramid there were / cases after blows in the temporoparietal area The pyramid falling to the pad possesses a kinetic energy and the ossicles possess their kinetic energy as well The energy of the ossicles is proportionate to the mass and squared speed and differs from the kinetic energy of the pyramid by the smaller mass When the pyramid remains intact after the fall it is stopped on the pad its velocity becomes zero and the whole value of the kinetic energy becomes zero too When the pyramid is fractured, it does not keep in total repose but it preserves some velocity and its kinetic energy has a certain value In both instances the ossicles try to keep their kinetic energy by the law of inertia The resulting drawing on the ossicles and their possible dislocation will be dependent

on the difference between the energy of the ossicles and that of the pyramid If the pyramid is not fractured this difference is greater as is the drawing on the ossicles. If the pyramid is fractured, this difference is smaller as is the drawing on the ossicles. With the blow on the pyramid the separate small parts of the bony tissue of the walls of the pyramid and of the ossicles vibrate and these vibrations are transferred in the travelling waves within the bones of the pyramid and ossicles. If these opposite waves strike one against another interference occurs and in some points the vibrati ns subside (nodes) while in other points the vibrations have their maximum (antinodes) When the pyramid is intact after the fall, the whole kinetic energy changes into the deformation energy This energy causes great vibra tion and a greater possibility of dislocation of the ossicles. When the pyramid is fractured the deformation energy is small because the majority of the kinetic energy is spent in producing the fracture, and therefore vibration and the possibility of di location of the ossicles are smaller These two mechanisms play the main role in the damage to the ossicular chain due to head injury without fracture of the pyramid

ZUSAMMENFASSUNG

I 30 Fallen wurde bei den nach tödli hen Schädeltraumen I rchgeführten Sektionen an den Schläf beinen festgestellt, d ss es bei den durch d Wände der Mittelohrhöhle erlaufenden Querfrakturen der Pyramid meist zu k inen Verletzu gen der Knöchelchenkett k mmt, während bei den ebenf lls durch lie W nde der Mitt lohrhöhle rlaufenden Längsbrüchen die K öchelchenkette fast regelmässig geschäd gt wird Nicht selten ist bei inem Schäd ltrauma di Knochelchenkett terbrochen, h dass es zur Pyramidenfraktur gekomm w re Auf Grund unserer Erf hru ge mit den nter erschieden n physikalischen Bedingu gen experiment ll durchgeführten Pyramidenfrakturen wird diese Tat sa he auf di untersch edliche Festigk it der Pyramidenwä d sowie uf unter schiedl h Wirkungsmechan sme zurückgeführt bei Längsfrakture wirkt sich die Schubkraft bei Querfrakturen di Zugkraft us. Die Knöchelche Dislokation be Schad l erletzu gen h Pyramidenfraktur wird ls F lge der Differe z w schen der kinetischen Energie der Knöchelchenkett *und der Pyrami le* ach dem Ei fall uf d Hi dern und I Ergebni der I terferenz der Def rm tionsw llen erklart, di h n ch dem Einfall auf I Hinderni d rch di Pyramid nknochen sowie durch die Gehörknöchelchen usbreiten

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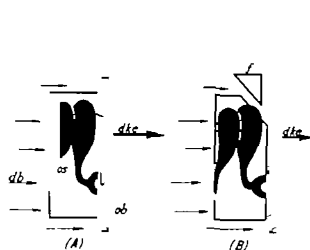


Fig 5

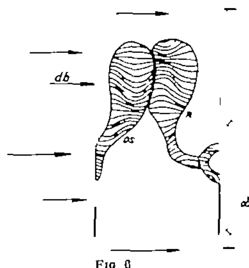


Fig 6

Fig 5 Kinetic energy of the ossicles due to blow of the pyramid on the obstacle. (A) Intact pyramid (B) fractured pyramid *db* Direction of blow *dk* difference between kinetic energy of the ossicles and the pyramid *f* fragment of the fracture *ob* obstacle *os* ossicle

Fig 6 Interference of the deformation waves, travelling through the ossicles *a* Antinode *db* direction of blow *n* node *ob* obstacle *os* ossicle

ened by the cellular system of the mastoid process, the pyramid in this direction is firm and safely protects the ossicles. The blow directed through the occipital area to the tympanic cavity does not disrupt the ossicular chain unless produced by excessively strong energy These facts explain the differences between our autopsy findings on the ossicular chain within longitudinal and transverse fractures of the tympanic cavity walls. The main factor in deciding whether the transverse fracture of the pyramid is associated with the damage of the ossicular chain or not is the energy by which the impact is carried out and the mechanism of fracture—not its location

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DETERIORATION OF THE RESIDUAL HEARING OF CHILDREN WITH SENSORINEURAL DEAFNESS

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From the Commonwealth Acoustic Laboratories Sydney Australia

Deterioration in the residual hearing of the aided and unaided ears of children with sensorineural deafness was investigated by comparing the mean Average Hearing Losses of their initial audiograms with the mean Average Hearing Losses of recent audiograms, and relating the changes to various variables. The results of the investigation confirm previous findings that the use of high-powered hearing aids tends to cause deterioration of the hearing of the aided ear, that this effect of aid use is about the same in degree in endogenous and exogenous deafnesses and that a small amount of deterioration of unknown origin tends to occur in the unaided ears of children with sensorineural deafness, and tend to be greater in ears with less initial hearing loss. It was also found that the general deterioration of hearing tends to be bilateral and greater in exogenous than in endogenous deafnesses.

In a previous investigation by Macrae & Farrant (1965) on the hearing progress of 87 children with sensorineural deafness, it was found that the use of high powered hearing aids tends to cause deterioration of the hearing of the aided ears. Deterioration of hearing was also found to occur on the average in the unaided ears of the children, and the results suggested that this general deterioration tends to be greater in ears with less initial hearing loss.

At about the same time as these findings were published Barr & Wedenberg (1965) published the results of an investigation in which they followed the hearing progress of 84 children for periods of up to 15 years from the first reliable hearing test.

The group was composed of 40 children whose hearing losses were endogenous in origin and 44 whose hearing losses were exogenous in origin. The exogenous group was sub-divided into children whose hearing loss had resulted from (a) maternal rubella, (b) perinatal accident, or (c) meningitis (with or without dihydro streptomycin treatment).

None of the 38 children with hearing loss due to maternal rubella or perinatal accident showed any progressivity of hearing loss in either the aided or unaided ear despite constant use of a hearing aid. (Barr & Wedenberg state that most of the hearing aids used by the children studied had output limits below 130 dB SPL.)

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D pt of Ot laryng logy Cha l s University H d c Králové C ech lovaki

R ceived July 5 1967

PROCEDURE

Subjects

The subjects of the investigation were 134 children with bilateral sensori neural deafness, ranging in age from 5 to 18 years.

Audiological records on the children were selected from the files of the Commonwealth Acoustic Laboratories (C.A.L.) New South Wales State Laboratory (which contains records on 1630 partial hearing children issued with hearing aids) on the basis of the criteria set out below All children satisfying the criteria were included in the study excepting those included in our previous investigation

Thirty-two of the children were using 5TA hearing aids, 40 were using 5TB aids, 38 were using TB aids, and 24 were using T3 hearing aids

The length of time from the first reliable audiogram obtained from each child to a recent reliable audiogram ranged from 1 year to 12 years, the mean length of time being 5.23 years

Criteria for selection of subjects

Children whose data were accepted for the investigation were required to have

(*a*) Sensorineural hearing losses in both ears.
(*b*) No conductive overlay in either ear
(*c*) No history of recurrent otitis media
(*d*) As f r as possible, hearing losses of approximately the same degree in each ear in the initial audiogram.
(*e*) At least 12 months regular use of a hearing aid
(*f*) No changes of aided ear or type of hearing aid
(*g*) One reliable audiogram at or near the beginning of use of hearing aid
(*h*) One recent reliable audiogram.
(*i*) An otolaryngologist s decision on the etiology of the deafness.

Information obtained from the records

(*a*) The A erage Hearing Losses (deri ed at C.A L., by calculating the mean loss through the three octaves from 500 cps t 4000 cps) in both ears from initial and recent audiograms.
(*b*) The dates on which initial and recent audiograms were taken, and the ge of the child
(*c*) The type of hearing aid used, and the ear in which it was used.
(*d*) The etiology of the deafness, as judged by an otolaryngologist.

Apparatus and testing m thod

All audiometric tests were carried out by audiological psychologists using a 5dB step descending threshold technique The audiom ters used were designed nd constructed at C.A L., and are calibrated to A.S.A standards. The acoustic output of the audiom ters is checked regularly to ensure that

TABLE 1 *Specifications of hearing aids used by children in this investigation*

Aid desig	Max. gain (dB SPL)	Max. acoustic power (dB SPL)
5 TA	30–36	115–117
5 TB	40–45	117–119
TB	45–50	120–124
T5	55–65	126–130

All of the 6 children whose hearing losses had been caused by meningitis showed deterioration of hearing in the aided ear In 5 of these children there was a total loss of hearing in the unaided ear but in the one child with residual hearing in both ears the deterioration was greater in the unaided ear Barr & Wedenberg consider it likely therefore, that the deterioration in the aided ears of the other 5 children is general deterioration and not due to hearing aid use

Twenty two out of the 40 children with endogenous deafness showed progressivity in hearing loss Of these 22 only 2 had been using a hearing aid regularly in one ear One of them had greater progressivity in the unaided ear and the other had the same degree of progressivity in both ears.

Other investigations previously carried out on the questions of the effect of hearing aid use on hearing and the general deterioration of the hearing of children with sensorineural deafness are adequately referenced in these articles by Macrae & Farrant and Barr & Wedenberg

In view of the discrepancy between Barr & Wedenberg's findings and our own, it was decided to reinvestigate the above questions, using a different (independent) sample from that used in the previous study On the basis of two considerations children using lower powered hearing aids were included in the sample Firstly it would enable us to investigate whether lower powered hearing aids have any effect on hearing, and secondly if there were no effect of using these aids we would be able to investigate the general deterioration of hearing in greater detail

The designation and power of the hearing aids used by the children in this study are given in Table 1

The aims of the investigation were

(1) To examine the hearing progress in the aided and unaided ears of children with sensorineural deafness who had been using hearing aids for some time

(2) To establish the degree of relationship between any changes in hearing found and any variables thought to be connected with these changes

PROCEDURE

Subjects

The subjects of the investigation were 134 children with bilateral sensorineural deafness, ranging in age from 5 to 18 years.

Audiological records on the children were selected from the files of the Commonwealth Acoustic Laboratories (C.A.L.) New South Wales State Laboratory (which contains records on 1650 partial hearing children issued with hearing aids) on the basis of the criteria set out below All children satisfying the criteria were included in the study excepting those included in our previous investigation

Thirty-two of the children were using 5TA hearing aids, 40 were using 5TB aids, 38 were using TB aids, and 24 were using T5 hearing aids.

The length of time from the first reliable audiogram obtained from each child to a recent reliable audiogram ranged from 1 year to 12 years, the mean length of time being 5.25 years.

Criteria for selection of subjects

Children whose data were accepted for the investigation were required t have

(a) Sensorineural hearing losses in both ears.
(b) No conductive overlay in either ear
(c) No history of recurrent otitis media.
(d) As far as possible hearing losses of approximately the same degree in each ear in the initial audiogram
(e) At least 12 months regular use of a hearing aid
(f) No changes of aided ear or type of hearing aid
(g) On reliable audiogram at or near the beginning of use of hearing aid
(h) One recent reliable audiogram.
(i) An otolaryngologist s decision on the etiology of the deafness.

Inf rm tion obtained from the records

(a) The Average Hearing Losses (derived, at C.A.L., by calculating the mean loss through the three octaves from 500 cps to 4000 cps) in both ears fr m initial and recent audiograms.
(b) The d tes n which initial and recent audiograms were taken and th age of the child
( ) The type of hearing aid used, and the ear in which it wa used
(d) Th etiology of the deafness, as judged by an otolaryngologist.

Apparatus and te ting method

All audiometric tests were carried out by audiological psychologists using a 5dB step descending threshold technique The audiometers used were designed nd constructed at C.A.L., and are calibrated to A.S.A standards The acou tic output of the audi meters is checked regularly to ensure that

TABLE 2 *Means of Averaging Hearing Losses in initial and recent audiograms of 134 children*

Type of aid	No of cases	Aided ears First A/G	Aided ears Recent A/G	Change in A H.L.	Unaided ears First A/G	Unaided ears Recent A/G	Change in A H L.	Difference between changes
5TA	32	40 9	45.1	4.2	43.5	47 8	4.3	– 1
5TB	40	50 7	51 6	3 9	53 1	55.9	2.5	1 4
TB	38	62.7	0 8	8 1	68 6	1.5	2.9	5.2
T5	24	81 6	90.2	8 6	89.3	90 0	1 6	0

significant at 01 level
ignificant at .05 level

it conforms to correct calibration standards The maximum output above normal threshold of the audiometers is 95 dB at 250 cps 105 dB at 500 cps and 115 dB at 1000 to 4000 cps

RESULTS

1 *Change of Average Hearing Loss (A.H.L) in Aided and Unaided Ears*

The means of the Average Hearing Losses derived from initial and recent audiograms were calculated for both the aided and unaided ears of the children The differences betwen the means were obtained by subtracting the initial audiogram mean from the recent audiogram mean The results of the calculations are given in Table 2

(1) Changes of A H L. in the aided and unaided ears of the children using 5TA and 5TB hearing aids are about the same

(2) Changes of A.H.L in the aided ears of the children using TB and T5 hearing aids are greater than the changes in their unaided ears

(3) Changes of A H L in the unaided ears of the children tend to be less in the groups with greater initial hearing loss

2 *Hearing Aid Effect in Endogenous and Exogenous Deafness*

The effect of hearing aid use on children using TB and T5 hearing aids was estimated for each individual by subtracting the change in A H L. in the unaided ear from the change in A H.L in the aided ear The children using TB and T5 hearing aids were then divided into those with endogenous (hereditary) and those with exogenous deafness, and the mean hearing aid effect was calculated for both groups. (Etiology was unknown for 18 of the children)

The results are given in Table 3

TABLE 3. *Mean change in A.H.L. attributable to aid use in aided ears of children with endogenous and exogenous*

Etiology	No. of cases	Mean change
Endogenous	11	6.23
Exogenous	33	6.03

The mean change in A.H.L. attributable to hearing aid use is thus approximately the same in the children with endogenous and exogenous deafness.

3 *Change of A.H.L. in Unaided Ears of Endogenous and Exogenous Deafnesses*

The children under investigation were divided into three groups on the basis of etiology those with endogenous deafnesses, those with exogenous deafnesses, and those with deafness of unknown etiology The mean change in A.H.L. in the unaided ears was then calculated for the children with endogenous and exogenous deafnesses.

The results of the calculations are given in Table 4

It is clear from this table that, in this sample of children, the average degrees of deterioration in exogenous deafnesses are consistently greater than those in endogenous deafnesses

In order to check whether this was due to large amounts of deterioration in small numbers of exogenous cases only the distributions of the

TABLE 4 *Mean change in A.H.L. of unaided ears of children with endogenous and exogenous deafnesses*

Aid group	Etiology	No. of cases	Mean change of A.H.L.
5TA	Endog.	11	1.5
	Exog.	14	6.0
5TB	Endog.	11	2.0
	Exog.	15	5.3
TB	Endog.	5	2.6
	Exog.	24	4.7
T5	Endog.	6	0.7
	Exog.	9	1.4
All cases	Endog.	33	1.7
	Exog.	62	4.4

Continued page 44

changes in A.H L in endogenous and exogenous cases were checked, and found to be the same in shape Thus the greater deterioration in the exogenous deafnesses is not attributable to small numbers of cases with large degrees of deterioration

4 *Correlations*

All correlations done were Pearson product moment correlations.

Correlations between changes in A H L in the aided and unaided ears of 5TA and 5TB cases were calculated (in these cases there is no discernible hearing aid effect) The coefficients obtained were

5TA cases $r = 68$
5TB cases $r = 53$

Inspection of the scattergrams revealed that the majority of cases had equal degrees of change in both ears and that almost all of the remainder were unilateral changes

CONCLUSIONS

1 The principal result of this investigation confirms our previous finding that the use of powerful hearing aids has a deleterious effect upon the residual hearing of children with sensorineural deafness. The mean amounts of deterioration attributable to hearing aid use found in this investigation correspond closely with those found in our previous study In the present investigation, an average of 5.2 dB of the deterioration in the aided ears of TB cases and 7 0 dB in the T5 cases, could be attributed to hearing aid use In the previous study the corresponding figures were 4 8 dB and 6 9 dB respectively

2 The effect of hearing aid use is about the same in endogenous and exogenous deafnesses This also confirms a similar finding in our previous investigation

3 On the average small amounts of deterioration were found in the unaided ears of the children The deterioration was less in children with greater degrees of initial hearing loss, again confirming a previous finding

4 In the unaided ears of the children the exogenous deafnesses consistently tended to deteriorate more than the endogenous deafnesses Why this should be so is not apparent, and the numbers of cases in the subclasses of exogenous deafness were too small for valid comparisons to be made However it was noted that *some* deterioration of hearing tended to take place in *all* the sub-classes

5 The deterioration not attributable to hearing aid use tends to be bilateral and equal in degree in both ears (and is unilateral in only a small number of cases)

ACKNOWLEDGMENT

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Verschlimmerungen der Hörrest in Ohren, mit und ohn Hörgerät bei Ki dern mit I ne hrschwe hörigkeit wurden d rchgeführt durch Vergleich der Durchschnittshörverl ste der Hörk rven mit dem Durchschnittshörverlust der Hörkurve jüngeren Datums, bezogen auf Änderungen durch erschiedene abhängige Variable Di Ergebnisse der Untersuchungen bestätigen frühere Funde nämlich dass stark Hörapparate da Hörvermögen des mit Hörapparat versehenen Ohres erschlechtern und dass diese Einfl ss von glei hem Ausm bei endogener wie exogener Schwerhörigk it ist weiterhin dass klein Verschlimmeru gen unbekannten U spru gs i den Ohren bei Kindern mit In enohrschwerhörigkeit ohne Hörapparat orkommen (diese Verschlimmerungen sind grösser bei kleinen Hörverlusten, wen zuerst geprüft) Man f d uch, das Gehörverschlechterungen, die nicht durch Hörapparate verursacht wurd die T denz hatten doppelseitig zu sein d dass sie bei ogener Schwerhörigkeit grösser w ren ls bei endogener

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SOME MORPHOLOGICAL OBSERVATIONS OF REISSNER'S MEMBRANE

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Light microscopic photographs of the dissected Reissner's membrane of an albino guinea pig were shown. Polygonal flat epithelial cells on the side of the scala media are larger on the outer side of the membrane than on the inner side of it. Between the outer and the inner sides of this membrane a transitional zone was noticed. Viewed from the inner side of the membrane, this zone—covering the area from the base to the apex—is nearer the base than the apex. It may be assumed that the outer larger cells are more active in their function than the inner smaller cells. There might also be reason to assume that the epithelial cells of Reissner's membrane grow larger as they move from the inner to the outer side of it.

The structure of the organ of Corti has been subject to many examinations. However, only little attention has been paid to Reissner's membrane because of its apparent morphological simplicity. Recently, this thin and special structure, separating the scala media from the scala vestibuli, has aroused much interest among oto-physiologists and oto-histologists. An excellent publication on this subject has recently been presented by *Rauch* (1964).

There are different theories on the function of this membrane. The foremost theory is that Reissner's membrane is permeable by active transport. Recently *Lawrence et al.* (1961) presented an excellent schematic drawing of this membrane's structure.

Up to the present, however, the morphology of Reissner's membrane could not clearly be demonstrated by light microscopy. It was to be expected that a sectioned specimen would not give a good picture of the entire membrane. Therefore, I believe it is necessary to dissect the specimen in order to get a three-dimensional picture of Reissner's membrane. It was the purpose of this study to obtain a light microscopic picture of the dissected membrane of the guinea pig's cochlea.

METHODS

The cochleas of 20 adult albino guinea pigs (average weight 300 g) were used for this study. The animals were anesthetized by intraperitoneal ad-

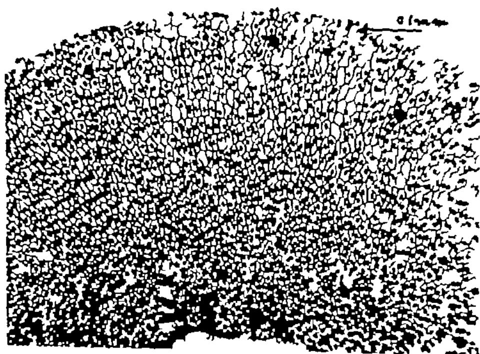


FIG. 1 Reissner' membrane viewed from the side of the scal media. Radially distributed flat epithelial cell are distinctly stained. A few scattered mall dark dots represent the nucl i of the mesotheli l cell hich re located on the ide f the scala vestibuli of Reissner's membrane Hematoxylin-eosi fter sil er reaction. Middle turn

ministration of sodiumpentobarbital (30 mg/kg) After decapitation the temporal bones were removed and immersed in a 0.2% $AgNO_3$ solution placing them for 15 minutes—the oval and the round window exposed—in a cold and dark chamber For nly a few seconds the cochleas were then wa hed with a 0.2% NaOH solution and afterwards fixed with 0.2% formalin for 24 hours. Using a sharp needle, pieces of Rei sner's membrane were dissected in a suitable length from the apex to the base of the cochlea These pieces were then treated with hematoxylin-eosin Some celloidin sec tion of Reissner s membrane were also studied. Photographs were taken at original magnifications of 150 to 800 and a micrograph was made for each enlargement

For measurement the a.m. dissected specimens were directly put on the objectmi romet r (Eleitz Wetzlar 1/100 m/m) Then the shortest distance from the inner to the outer edge of Reissner s membrane in the middle of each turn of the cochlea was measured. For this measurement Reissner's membrane was not distended.

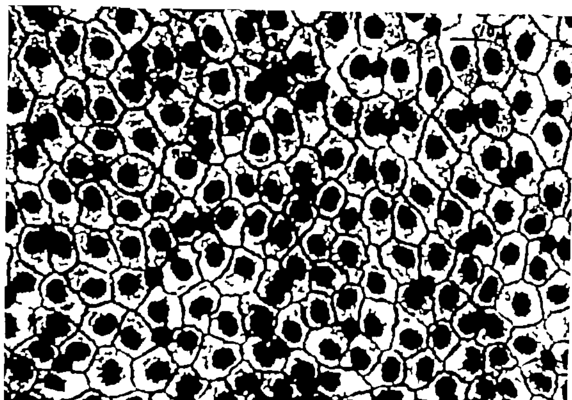


Fig 2. Flat pith lial cells on th inn side f R issne membrane Th nu lei nd cell membranes are learly dem n trated. Hematoxylin-eo in aft r silve reacti n. Middl turn

OBSERVATIONS

Regarding the cells of Reissner s *membrane, only two groups of different* origin have hitherto been discovered firstly the polygonal flat epithelial cells of ectodermal origin facing the endolymph and, secondly the mesothelial cells of mesodermal origin facing the perilymph According to an electronmicroscopical study of Iurato & Taidelli (1967) Reissner s mem brane measures 2–3 μ in thickness and a distinct basement membrane is 400 Å thick, some intercellular substance being interposed between the epithelium and the mesothelium

Flat epithelial cells (Fig 1) forming a single layer on the side of the scala media show a good radial arrangement from the spiral limbs to the spiral ligament The cell membranes and nuclei are distinctly stained The *cell membranes are somewhat notched (this may be a fixation artifact)* The nucleus is oval and located in the very center of the cell

According to Iurato & Taidelli (1967) the epithelial cells of Reissner s membrane show microvilli and pinocytotic vesicles on their endolymphatic surface The latter contain some dense material and have a bristle coat on their convex cytoplasmic side The basal part of the epithelial cells is often equipped with fine cytoplasmic processes They are separated by large

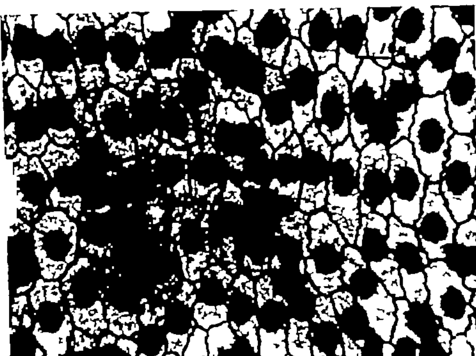


Fig. 3. Fl t epithelial cell f the outer side of Reissner' membra It ppears if they are grow ng tow rds the outer side f R iss er' membrane. H mat xylin-eosin fter all er reaction Middl turn.

intercellular spaces and cover the basement m mbrane Here also, some pinocytotic vesicles similar to those described on the endolymphatic surface can be noticed. The cytoplasm contains the oval nucleus, vesicles, tubules, free ribosomes, some mitochondria, a small Golgi apparatus, some filaments and a few pigment granules

As shown in Fig 1 the epithelial cell on the inner side (Fig. 2) of Reiss ner membrane are smaller than those on the outer side (Fig 3) The size of the transitional zone between the smaller and the larger cells, however cannot clearly be d fined. This zone is more distinct in the lower than in the upper coils. In the basal coil the larger and the smaller cells are ar ranged in rows with only a very small transitional zone The cells on the outer side of Reissner s membrane are radially elongated and rectangular containing more cytoplasm than those on the inner side of the membrane The cells on the inner ide are irregularly distributed and more pentagonal in shape Light microscopical pi tures did not yield any pigment granules and cell excrescences in the epithelial cell layer

On the other h nd are the mesothelial cells (Figs. 4 and 5) forming a si gl l yer on the side of the scala vestibuli, variable in shape some being

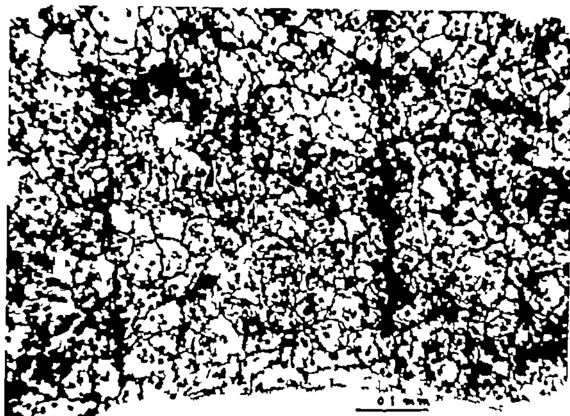


Fig 4 R issner s m mbrane viewed from the id f the sc la vestibuli Th mes thell l cell re very large d irregula ly di tributed No region l diff rence re detectable Hem toxylin-eosin fter ilver reacti n Middl turn

elongated and others round The mesothelial cells are a few times larger than the flat epithelial cells The sectioned specimen shows that the mesothelial cells are much thinner than the flat epithelial cells The nuclear portion of the cell is raised to the free surface The nucleus of the mesothelial cell is smaller than that of the epithelial cell The cytoplasm contains few organelles but several pinocytotic vesicles with a simple clean limiting membrane (Iurato & Taidelli 1967) Light microscopy did not reveal any pigment granules in the mesothelial cell layer Concerning the mesothelial cells, there were no characteristics and significant differences in any region throughout Reissner s membrane

Fig 6 is a schematic diagram representing the whole Reissner s membrane viewed from the side of the scala media The beginning of the third turn of Reissner s membrane narrows towards the apex and the base On the outer edge of Reissner s membrane one row of spirally arranged epithelial cells is found connecting the membrane with the stria vascularis The sectioned specimen seems to reveal that the outer edge of the membrane leads into the bottom part of the stria vascularis. The stria vascularis contains 4 different cell groups (Smith 1957 Engström *et al* 1955) the

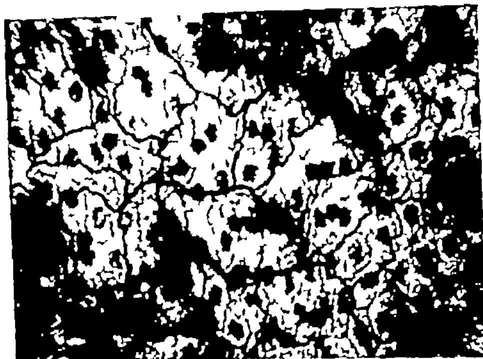


FIG. 5. A highly magnified photograph of the mesothelial cell of Reiss er' membrane These cells re several times larger than the epithelial cells. Th nucleus of mesothelial cell, ho ever i smalle tha that of epitheli l cell H mat xylin-eosi ffer ll er reaction. Middl turn.

marginal (dark) cells, the intermediate (light) cells, the basal *cells*, *and* the endothelial cells of the blood capillaries. The basal cells are located in the bottom part f the stria vascularis they intricately interdigitate with the marginal cells and the intermediate cells. The epithelial cells on the outer edge of th membrane seem to be connected with the basal cells *of the* stria vascularis.

The directly measured width of Reissner's *membrane* in 20 examined adult animals (average weight 300 g) reads as follows

Turn	I	II	III	IV
Mean size (mm) in the middle of each turn	0.50	0.50	0.51	0.44

Another significant and characteristic feature of Reissner's membrane in the guinea pig is that the area, covered with the outer larger epithelial cells, is wider in the basal coil. This area gradually narrows towards the apex. The area covered with the inner smaller *epithelial* cells, on the other hand, i smaller in the basal coil and gradually widens towards the apex.

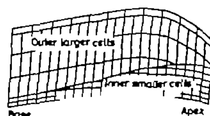


Fig 6 A schematic drawing of R issner's membrane viewed from the side of the scala media N te that one row of epithelial cells connects the membran with the stria vascularis The area f the oute larger epithelial cells I wider in the base narrowing *towards the apex of the cochlea*

COMMENTS

Since Reissner *in 1851 first discovered the membrane which separates* the scala media from the scala vestibuli of the cochlea many examinations have been made as regards the structure of this membrane

Retzius in 1884 studied Reissner s membrane in humans and sketched the two cell groups the mesothelial spindle-shaped, single-layered cells which often show pigment granules and appear on the side of the scala vestibuli, and the single layer of polygonal flat epithelial cells which lengthen here and there and which are vertically arranged The latter often suggest yellow pigment granules appearing on the side of the scala media

Quite often excrescences or protuberances were observed on the epithelial cell layer of Reissner s membrane in humans. These excrescences or protuberances *are in some cases regarded as an ordinary feature* while in other cases these phenomena are considered pathological alterations Retzius (1884) termed them rundliche oder traubenförmige Vorsprünge" and did not believe them to be pathological alterations Wustrow (19›2) detected them even in fresh materials of the human inner ear and called them "Buckel" or Warzchen

Excrescences, however were also found in the vestibular part of the labyrinth Rüdinger (1867) called them "Zotten when appearing in the semi-circular canal of the normal human cochlea Hallpike & Cairns (1938) and Altmann & Fowler (1943) designated this phenomenon a subepithelial vesiculation when found in the saccule and the semi-circular canal of the inner ear in cases of Menière s disease Lempert *et al* (19›?) also believed that these vesiculated epithelial excrescences or globules in the epithelial lining of the vestibular labyrinth have a bearing on the formation of epithelial fluid collections, and are undoubtedly of pathological significance in Meniere s disease However as far as we know the structure of the vestibular part of the endolymphatic wall is different from the structure of *the cochlear* part of the endolymphatic wall It may therefore be assumed that these epithelial excrescences or protuberances in the vestibular labyrinth are a different problem altogether

Observations recently made by Lawrence *et al* (1961) electron-microscopical studies made by Bairati & Iurato (1964) and the present experiments have all been quite informative as to the morphology of Reissner s membrane even though much of it still remains unsolved

We confirm that Reissner s membrane in the guinea pig contains two different cell groups (1) Polygonal flat epithelial cells facing the endolymph and (2) mesothelial cells facing the perilymph. However we were not able to find any spindle-shaped mesothelial cells but did detect rather large mesothelial cells which were of irregular shape Pigment granules and cell excrescences, however were not noticed in Reissner s membrane in tested albino guinea pigs. Savin (1965) studied the interrelationship between blood vessels and pigmentary cells of the guinea pig as well as those of humans (white-skinned and natives of Mexico) He dissected the inner ear and observed th distribution of the pigments in the connective tissue zones near the elements of a very intense specific activity (the stria vascularis, the spiral ligament the modiolus, Reissner s membrane and the planum semilunatum of the cristae)

According to Savin (1965) pigmentary cells of Reissner s membrane could not be discovered in histological sections of temporal bones (Wolff 1931) Their shape is variable and shows in some cases three prolongations. They spread unevenly covering only 2/3 of the membrane Savin was not able to detect any pigment granules in the labyrinth of the albino guinea pig

On the evidence of my studies and the microscopical photographs of Reissner s membrane in the guinea pig, I conclude that thi membrane is wider in the beginning of the third turn, and that it gradually narrows towards the apex and the base

It i pos ible that the epithelial cells of Reissner s membrane grow larger as they move from the inner to the outer side of the membrane and that th inner smaller epithelial cells in the lower coils will reach their full size sooner than those in the upper coils. Furthermore there is reason to assume that the outer larger cells are more active in their function than the inner smaller cells

ACKNOWLEDGMENT

I would lik t xpress my i cere gratitude t Prof D S Katagiri a d hi as istant Prof Dr K Kaw moto, as well Dr Y Kaneko and Dr K Hori \ pecial w rd of thanks goes t Prof Dr S Rauch (Düsseldorf Germany) who ha provided me with extremely valuable help especially in publishing thi work. I also wish t pres my thank to Miss A. Rupert wh did the translation

ZUSAMMENFASSUNG

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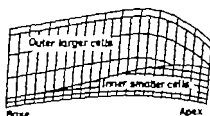


Fig 6 A schematic drawing of Reissne s membrane viewed from the id of the scal media Note that one row of epithelial cells connects the membrane with the stria vascula I The area of the outer larger pithelial cells is wid in th base narrowing towards the apex of the cochlea

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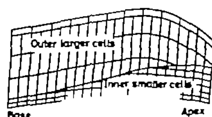


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AUDITORY FUNCTION IN DIABETICS

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Assessments of the hearing in diabetics by means of simple clinical test and at times also by pure tone audiometry have yielded the most conflicting results. In published surveys the frequency of sensorineural hearing impairment has varied between 0 and 80%. It was therefore felt desirable to investigate this clinical problem applying modern audiological tests, which so far has not been done. Ninety-nine relatively young known diabetics have been examined. Pure tone audiograms were normal considered as group means. A small but definite degree of hearing impairment was noted when the patients were tested by speech and distorted speech audiometry as well as by Békésy and directional audiometry. In view of the psychoacoustic nature of the latter tests, all results were critically evaluated. No correlations were noted between the recorded hearing loss and the duration or severity of diabetes. Greater hearing losses were however directly related to higher age. The sexes were similarly affected. The significance of the results is discussed.

Middle ear suppuration was common in the preantibiotic era, particularly in less well nourished people. Extension of the disease to involve the brain, the labyrinth and the blood stream was dreaded. The course was often rapid and fulminating and the mortality high. Of necessity extensive operative procedures were carried out on the ear in an attempt to check progress of the disease. This often resulted in even greater hearing losses, in many cases in almost total deafness. In the uncontrolled diabetic with generalised low body resistance and with tissues very prone to infection the prognosis was still worse.

With the discovery of insulin in 1922 and the advent of the sulfonamides and antibiotics, many cases of otitis media in diabetics were cured. Any residual perceptive deafness could then be attributed to labyrinthitis.

Gradually reports appeared demonstrating that hearing in diabetics sometimes was impaired without a history of middle ear suppuration. A compilation of these investigations is presented in Table I. It shows that only simple hearing tests, and at most pure tone audiometry, had been performed. No attempts were made to perform a topical analysis of the hearing impairment, i.e. to analyse if the lesion was cochlear or retro-cochlear.

[illegible] supported by Grant from the Research Fund of the Swedish Diabetic Association and by AB Hässle, Göteborg.

weist polygonale flache Zellen auf die in Modiolusnähe klein und zur lateralen Cochleawand hin immer grösser werden Dieser Übergang von kleineren zu grösseren Zellen liegt in der Asalwindung stark median um nach spikal hin sich immer stärker nach lateral zu verschieben Die mesodermalen Zellen zum Perilymphraum hin sind wesentlich grossflächiger Dieser morphologische Unterschied lässt auf eine unterschiedliche Funktion schliessen Zudem kann aus der Anordnung der kleinen und grösseren Zellen der endolymphnahen Schicht geschlossen werden dass wahrscheinlich diese Epithelien von der Modiolusseite aus in radialer Richtung *zur Peripherie hin wachsen und dass die schmalen* Zellen in den basalen Windungen sich schneller in grosse Zellen umwandeln

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be due to presbyacusis. The possibility that hearing impairment in diabetics might be due to involvement of the central auditory pathways has so far escaped recognition.

Furthermore some investigators have attempted to correlate hearing loss and various late diabetic manifestations. The results of these investigations are given in Table 1 and also appear contradictory.

A compilation of published theories on the *aetiology* of inner ear damage in diabetics is presented below.

	Presumptive aetiology
Wittmaack (1907)	Neuritis of acoustic nerve
Hegener (1908)	Neurolabyrinthitis or haemorrhage
Bruhl (1912)	Acoustic nerve damage by circulating toxin
Edgar (19[illegible]1)	Supports Bruhl and suggests the possibility of ischaemia due to endarteritis of internal auditory artery
Wertheim (1924)	Supports Bruhl & Edgar
J[illegible]noli & Delljanni (1936)	
Jörgensen (1961)	Angiopathy of inner ear
Zelenka & Kozak (196[illegible])	

Haemorrhage in the labyrinth or within the acoustic nerve has been supposed to cause sudden deafness in diabetics (Hegener 1908, Jörgensen, 1960).

Progressive ischaemic changes in these structures associated with degenerative arterial disease have been held responsible for cases of insidious hearing loss.

However in 1964 Dietzel suggested that diabetes could cause ischaemic changes that need not only be confined to the end organ of hearing or its nerve but might also involve central auditory pathways in the brain. In postulating this Dietzel held a broader view in appreciation of the fact that diabetes is a generalised disease but performed no hearing tests aiming to demonstrate retro-cochlear lesions.

Histopathological observations of the inner ear in diabetics have demonstrated a number of changes. Haemorrhages in the cochlea were found by Steinbrügge (1891). Degenerative changes in the acoustic nerve, in the spiral ganglion and in the organ of Corti were demonstrated by Wittmaack (1907) and Panse (1907). Vos (1931) also found pronounced atrophy of all parts of the inner ear. Jörgensen (1961) examined 22 inner ears from diabetics. He demonstrated severe PAS positive (periodic acid-Schiff stainable) thickening of the capillary walls in the stria vascularis. He was able to correlate his findings to similar changes in the vessels of the retina, kidneys and lower extremities and in certain cases in the vessels of the acoustic nerve in patients with late diabetic manifestations. Recently Costa (1967) examined the inner ears of albino rats with alloxan induced diabetes com-

TABLE 1 *Examination of hearing in diabetics*

Author	*Year*	Number of cases	Age in years	*Method*	Hearing impairment due to d.m. %	Correlation between hearing impairment and.	No correlation between hearing impairment and.
Kulz	1890	700			41		
Edgar	1951	15		Tft	14	Age severity of d.m.	Sex
Jannulis & Del Jannis	1936	74		Ww Sv Tft	39		Severity of d.m.
Camisasca	1950	81	2–75	Pta	40	Sex (men), duration and severity of d.m.	
		11	<30		0		
Vigi	1950	30	30–50		20		
		109	>50		81	Age	
Marullo	1950	100			ca 50	Blood pressure	Severity of d.m.
Borsak *et al*	1950	108	All	*Pta*	33	*Duration and* severity of d.m.	
Schröder	*1954*	297	*All*	Wv Sv Pta *(10%)*	*0*		
Kindl	1955	8000			0		
Ancona	1956	27	16–33	Pta	70		Severity duration of d.m.
Profazio & Baravelli	1959	18	<44	Pta	0		
		8	51–60	Pta	26		
		14	61–70	Pta	37	Ag	
Jorgensen & B h	1961	69	All	Pta	41	Ag reti opathy	Durati n, neuropathy blood pr
Di tzel	1962	849		Pta	5	Sex (m n) ag angiopathy	Duration dose of insulin, retino- nephro- neuropathy
Zelenka & K zak	1965	17	8–10	Pta	6	Duration angiopathy	

S = Spok n ice W = whi pered ice Tft = tuning f k test, Pta = pure t udiogram d m = diabetes m llitus.

However means of testing retro-cochlear hearing have not long been available Varied degrees of hearing loss were detected in up to 80% of those tested but with contradictions most difficult to explain In addition to the findings in Table 1 it may be stated that the hearing impairment in general was symmetrical *sensorineural high tone loss of insidious but* sometimes sudden onset (Jorgensen, 1960) in the latter cases often resulting in total deafness In diabetics with apparently normal ears sensorineural *deafness* usually manifests itself relatively late This could be assumed to

I *Clinical Examination*

All patients were routinely examined. The following diabetic manifestations were noted

1 *Rethinopathy of diabetic type*

2 *Nephropathy* Constant proteinuria without signs of infection (negative bacterial urine culture) was considered ascribed to diabetic nephropathy

3. *Peripheral angiopathy*

A *Skin temperature* of the toes wa measured after indirect heating When vascular changes are present which may be due to diabetes mellitus, the warming up of the toes is delayed due to defective vasodilatation (For normal and abnormal values see Brattgård *et al* (1951))

B *Abnormal oscillometry* Oscillometry was performed on the lower extremities with a Recklinghausen Oscillometer The oscillatory excursions in the ankle were measured and the patient s response was considered abnormal if these were remarkably small (0–0.5 units) or appreciably smaller than those in the wrist.

C. *Arterial calcifications* in the lower extremities were demonstrated in radiograms

D *Microangiopathy of the skin.* Histopathological examination of kin biopsy specimen was performed according to Säve-Söderbergh *et al* (1957) The most characteristic change in dermal microangiopathy is a thickening [illegible] the wall in capillaries and venules Thi lesion can also far less frequently be seen in non-diabetics. When two examinations deviated from n rmal the patient was considered to have peripheral angiopathy

4 *[illegible]uropathy* was based on the following examinations

A Routine clinical neurological examination

B. Electromyography

C Conduction velocity in a mot r nerve of the lower leg determined according t Fagerberg *et al* (1963)

D *Ele troencephalography*

Neuropathy was diagnosed on the f llowing criteria: There had to be at lea t two eurological symptoms or signs typical of diabetic neuropathy (e.g. Achilles areflexia and impaired vibratory perception in the lower legs) alt rnatively abnormal conditions in tests B, C, or D

O ly two of the patients had a serum cholesterol level of more than 300 mg per 100 ml The others had normal values less than 300 mg per 100 ml

Patients with a blood pressure of 150/100 and over were considered hypertensive

All patients were stabilised on insulin except two, who were on tolbutamide

Re ults of the Clinical Examination

In thi paper all the linical examination which were performed will not be discu sed in detail but all result are given in Table 2. The frequency

paring the vascular changes with those of six human diabetics PAS positive thickening of the vascular walls was demonstrated in both animals and men in the modiolus and the stria vascularis

No marked structural changes were observed in the organ of Corti, ganglion cells or nerve fibres

The problem

The survey of the literature exhibits the following interesting and conflicting points

1 Some clinicians have not been able to detect any form of sensori neural hearing impairment in diabetics while others have reported hearing loss in up to 80% of the subjects

The present investigation was designed to determine the frequency of hearing impairment in diabetics

2 An explanation for the very different results may have been the age of the patients tested i e series with high frequency of hearing impairment may have included a greater number of elderly people

The present investigation aims to perform hearing tests in fairly young diabetics to avoid presbyacusis as much as possible

3 Published reports do not define normal hearing" and have not presented any control series

The present investigation aims at defining "normal" and abnormal hearing in the different tests performed and to compare the results of the hearing tests with those of a corresponding series of non-diabetics.

4 Hitherto only pure tone audiometry has been performed No attempts have been made to establish if the hearing impairment was cochlear or retro-cochlear

The present investigation includes modern audiological tests aiming at differentiating cochlear and retro-cochlear lesions.

5 The literature exhibits many contradictions concerning the correlation between hearing impairment and diabetic manifestations

The present investigation evaluates critically the correlations between the hearing impairment and the diabetic state

MATERIAL AND METHODS

Three groups each consisting of 33 controlled diabetics were chosen at random from patients attending a diabetic out patient department for routine checks Group A was 10–30 years of age Group B between 30 and 39 years of age Group C between 40 and 50 years of age The present investigation was carried out on 59 men and 40 women Conventional statistical methods were applied The clinical and audiological investigations were carried out as follows

measured using band-pass filters 640 and 2000 Hz in series. According to Lindén P^{95} of a normal population have a discrimination better than 80% of the 43 words tested 40 dB above the hearing threshold for spondees. All patients tested

E. *Stapedius reflex test* Recording of the stapedius reflex threshold with impedance audiometry for the frequencies 250–500–2000–4000 Hz. Examined in 72 of the 99 patients.

Apparatus Madsen Acoustic Impedance Meter Type Z 061

The following are limit values of the normal series (Anderson & Wedenberg)

Hz	250	500	1000	1500	2000	3000
dB	90	90	90	95	90	90

If the stapedius reflex is elicited at a higher level in four of these frequencies, this was considered abnormal This corresponds statistically to P^{95} of the normal individuals.

F *Békésy audiometry* Tested for both continuous and intermittent tone 36 patients tested on a copy of the original Békésy audiometer 61 on the Grason–Stadler audiometer

In the present investigation the spikes in the audiogram were transformed to an average excursion expressed in dB The statistical analysis was made on patients tested with the Grason–Stadler audiometer

The Békésy audiometer provides information concerning auditory sensitivity differencelimen for intensity changes and adaptation. When the excursions do not exceed an average of 3 dB this has been considered a sign of cochlear involvement There is, however also normally a highest level of the excursions in the Békésy audiometry lying within the limits 6–12 dB This was confirmed by a corresponding non-diabetic series in the present investigation Higher excursions may be abnormal (see further under Comments)

G *Directional audiometry* Ability of sound localisation according to Nordlund (1963) Ninety two patients tested, 5 patients excluded because of visual disturbances.

Type of sound	Normal values (arithmetic mean of angular deviation)		Standard deviation
Pure tone 500 Hz	−10	3	±12
Pure tone 2000 Hz[a]	−30	+20	±21
Pure tone 4000 Hz[a]	10	+12	±10
Bandpass filtered noise movable head[b]	6	8	±6
Bandpass filtered noise-fixed head[b]	6	8	±6

[a] Average of 20 measurements
[b] Average of 10 measurements.

TABLE 2 *Number of diabetic complications*

Number of patients	33		33		33		99	
Age group years	16–30		30–39		40–50			
Mean duration of diabetes years	10.4		10.0		14.0			
Complications	Male	Female	Male	Female	Male	Female	Male	Female
Retinopathy	6	4	15	7	9	9	30	20
Nephropathy	2	3	7	4	3	3	12	10
Peripheral angiopathy	4	1	7	5	3	7	14	13
Hypertension	0	0	3	2	4	2	7	4
Neuropathy	5	8	11	7	7	10	23	25
Total number of complications	17	16	43	25	26	31	86	72
Total number of patients affected	9	8	17	9	10	13	36	30

of late diabetic manifestations compare well with other diabetes mellitus series of the same age and duration of disease. Thus the series can be considered representative of an average diabetic population of the same age.

II *Audiological Examination*

All patients were examined according to the following scheme:

1. *History* of hereditary deafness and hearing impairment, vertigo, tinnitus, previous ear disease, *exposition to noise and ototoxic agents.*

2. *ENT examination.*

3. *Audiological tests.*

A. *Spoken voice, whispered tests. Tuning fork tests.*

B. *Pure tone audiometry.* Air conduction 250–8000 Hz, bone conduction 250–4000 Hz. All patients tested.

Apparatus: Amplivox Audiometer Standard Model 025 and 438, calibrated according to ISO Standard.

Normal values: Group means for "normal" hearing according to the age and sex groups of the 1954 Wisconsin State Fair Survey (Glorig *et al.* 1957). Correction for difference in calibration was introduced.

C. *Speech audiometry*, i.e. speech discrimination test according to Lidén (1954) (Swedish monosyllabic phonetically balanced word lists). According to Lidén P_{95} of a normal population have a discrimination better than 94% of the 50 words tested at 30 dB sensation level. All patients tested.

D. *Distorted speech audiometry* according to Lindén (1960, 1964). The monaural ability to discriminate frequency distorted filtered speech is

measured using band-pass filters 640 and 2000 Hz in series. According to Lindén P^{95} of a normal population have a discrimination better than 80% of the 45 words tested 40 dB above the hearing threshold for spondees. All patients tested.

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Type of sound	Normal values (arithmetic mean of angular deviation)	Standard deviation
Pure tone 500 Hz	−10 3	±12
Pure tone 2000 Hz	−30 +20	±21
Pure tone 4000 Hz[a]	−10 12	±16
Bandpass filtered noise-movable head[a]	−6 8	±6
Bandpass filtered noise fixed head[b]	−6 8	±6

[a] Average of 20 measurements.
[b] Average of 10 measurements.

TABLE 2 *Number of diabetic complications*

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Age group years	16–30		30–39		40–50			
Mean duration of diabetes years	10 4		16 0		14 0			
Complications	Male	Female	Male	Female	Male	Female	Male	Female
Retinopathy	6	4	15	7	9	9	30	20
Nephropathy	2	3	7	4	3	3	12	10
Peripheral angiopathy	4	1	7	5	3	7	14	13
Hypertension	0	0	3	2	4	2	7	4
Neuropathy	5	8	11	7	7	10	23	25
Total number of complications	17	16	43	25	26	31	86	72
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2 *ENT examination*

3 *Audiological tests*

A *Spoken voice whispered tests Tuning fork tests*

B *Pure tone audiometry* Air conduction 250–8000 Hz, bone conduction 250–4000 Hz All patients tested

Apparatus Amplivox Audiometer Standard Model 625 and 438 calibrated according to ISO Standard

Normal values Group means for normal hearing according to the age and sex groups of the 1954 Wisconsin State Fair Survey (Glorig *et al* 1957) Correction for difference in calibration was introduced

C *Speech audiometry* i e speech discrimination test according to Lidén (1954) (Swedish monosyllabic phonetically balanced word lists) According to Lidén P₉₅ of a normal population have a discrimination better than 94% of the 50 words tested at 30 dB sensation level All patients tested

D *Distorted speech audiometry* according to Lindén (1960 1964) The monaural ability to discriminate frequency distorted filtered speech is

TABLE 3 *Number of patients with hearing abnormalities due to diabetes*

Individual analysis.

Testing method	16–30 years		30–39 years		40–50 years		Total	
	M	F	M	F	M	F	M	F
Pure tone audiometry	0	2	1	1	1	1	2	4
Speech audiometry	5	4	10	2	9	4	24	10
Distorted speech audiometry	7	7	4	5	7	10	18	22
Bék‑sy audiometry[d]	1	2	6	2	7	5	14	10
Directional audiometry	0	0	1	0	4	2	5	2
Stapedius muscle reflex[f]	5	9	1	0	2	0	8	0
Total number of abnormalities	14	15	23	11	30	22	60	48
Total number of patients affected	21/33		20/33		27/33		68/99	

Abnormal when the he ring threshold one more than ne frequency exceeded 15 dB of the group me

Abnormal whe discrimin tion was 94% or less one ea

Abnormal when discrimination w 80% or less on one ear

Abnormal when the mea excursion xceeded 12 dB

Abnormal when patient f ll out de (probability les 1) P = 99.9% (page 55)

f Abnormal when reflex threshold ceeded les ls specified on 4 frequencies (page 53)

In the individual analysis, when compared to the normal the three age groups included a significantly higher number of individuals with a dis crimination f r speech less than 94% on one or two ears, the lowest level 1⁰⁰ *accepted as normal in the present investigation (Table 3)*

The mean *discrimination for distorted speech* in the three age groups were respectively 81.5±2 1% 84 ±2.0% 82.1±2 4% *(group mean ±2×*

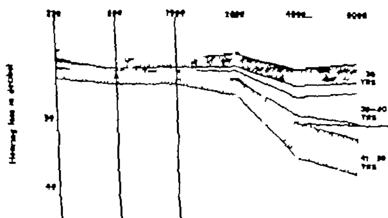


FIG. 1 Pure tone adiometry f diabetics. Confidence limit withi which f ll 95% of the bject tested, 33 subject i each group. Normal unselected cases f ll withi the confidence limits.

Abnormal values Patients who fall outside the above given values representing *P* 99 9

Audiological examinations of this kind are affected by various sources of error Most examinations were made in the late afternoon or evening after a day s work when many patients seemed tired and some unable to concentrate For most subjects the motivation for examinations of this kind was not very high and particularly patients long suffering from the disease showed obvious signs of irritation and fatigue The results of the audiological examination thus probably do not demonstrate the best possible hearing To reduce these disadvantages, always present in psycho-acoustic measurements the patients were offered the possibility of being tested on two separate occasions, and were examined by the same audiologist always attempting to test the patients in as good condition as possible More than half of the subjects were thus tested on two separate occasions

Results of the Audiological Examinations

The results of the audiological tests were considered in two ways First each age group was treated as a group and only group means considered No attention was paid to the individual s history Hence this should be a proper series for comparison with a corresponding non-diabetic and non selected series Secondly in the section on the correlation between hearing impairment and diabetes, every case was considered in relation to the individual s history i e any hearing impairment in pure tone audiometry related to exposure to ototoxic agents previous ear diseases and noise Only those hearing defects which could not be attributed to any such cause were regarded as due to diabetes (Table 3)

Tuning fork tests and results of conversation and whispered voice tests did not deviate from what further audiological findings demonstrated Only 10 of the 99 patients had subjective hearing loss and none of these were in the youngest age group Furthermore four of these 10 patients had normal findings in the tests. Twenty two patients experienced tinnitus but only 6 of these had hearing impairment

The results of the *pure tone audiometry* are given graphically in Fig 1 All cases, irrespective of previous audiological history were considered The results were compared with those of a corresponding population, i e an unselected non-diabetic population The figure demonstrates that pure tone audiometry in diabetics below 50 years was normal in the present series The limits of the individual analysis are given in Table 3 Six patients fell outside these limits exhibiting hearing impairment in pure tone audiograms without any other reasonable explanation than diabetes

The mean *discrimination for speech* in the three age groups were respectively 97 ± 0 9% 96 ± 1% 95.2 ± 1% (group mean ± 2 × standard error of the mean) With the limits given the three age groups lie within the normal values but the oldest exhibits an abnormal deviation

TABLE 4 *Correlation between hearing impairment and severity of diabetes*

Testing method	Abnormal audiometry due t diabetes in the 33 patient lth most diabetic complications, 11 from each age group	Abnormal diometry due t diabetes in the whole series, 99 patients
Pure tone audiometry	9	11
Speech audiometry	30	31
Distorted speech audiometry	52	40
Stapedius muscle reflex	6	6
Békésy-audiometry	27	21%
Directional udiometry	6	7

all values outside the given limits are contained in the following figures irrespective of histories.

The results may be presented as follows

I *Age* The present investigation demonstrated that there is a significant number of diabetics exhibiting hearing abnormalities (Table 3) The risk of being more afflicted by hearing disorders increases with age It is to be expected that the risk for the diabetic may be even greater when sensorineural loss due to aging is added.

From Table 3 it can also be seen that the number of patients demonstrating hearing impairment in two or more tests increases with age

II *Sex* In general it may be said th t sexes showed no differences (Table 3)

III *Duration f diabetes mellitus* No positive association can be drawn between any form of hearing defect and the duration of the disease whether considered indi idually or as a group

IV *Severity of diabetes mellitus* The clinical and audiological examinations made it possible to make an attempt at determining any associations that might xist between the severity of diabetes mellitus and any hearing disorder demonstrated

When the number of abnormal hearing tests in those 11 patients constituting of th age group most afflicted by different diabetic complications was compared to the total number of abnormal hearing tests in the whole series, no correlation could be demonstrated (Table 4) Even when turning the analysis and regarding each individual with any form f hearing impairment to evaluate if he was more afflicted by late diabetic complications, no correlations could be demonstrated.

Furthermore some of the late diabetic manifestations i.e. retinopathy and microangiopathy of the skin were graded according to severity Nor does an nalysis to demonstrate any correlation between hearing disorders and the severity f angiopathy in terms of these parameters indicate any correlation The abo findings thus indicate that no association existed between the severity f the diabetic process and hearing.

V *Lat liabetic complications* In none of the three age groups nor in

standard error of the mean) With the limits given the three age groups lie within the normal values but the youngest and oldest age groups exhibit an abnormal deviation

In the individual analysis, when compared to the normal the three age groups also included a significantly higher proportion of individuals with a discrimination for distorted speech less than 80% on one or two ears, which represents the lowest level P^{95} accepted as normal (Table 3) Thus there seems to be a slightly reduced discrimination for speech and distorted speech in the present series

In the *stapedius reflex test* only the individual analysis was performed No signs of cochlear involvement were demonstrated by the test The stapedius reflex level was recorded at a higher stimulation level than normal without signs of transmission fault in three cases in the youngest, in one in the intermediate and in two in the oldest group (Table 3) In six patients the stapedius reflex could not be recorded in spite of 110 dB sensation level With the normal values given only the youngest age exhibited a higher number of cases than could be expected The figures though are too small for statistical analysis

In *Békésy audiometry* the mean excursions in the three age groups were respectively 10.3±0 8 dB 13 2±1 7 dB 12±1.2 dB (group mean ±2× standard error of the mean)

This interesting finding that the diabetics have greater excursions in the Békésy audiograms was confirmed when the diabetics were compared to a corresponding non-diabetic series.

In the normal series the excursions of the subjects were within 6–12 dB (P^{95}) In the individual analysis the present series exhibits a high number of diabetics with greater excursions (Table 3)

No abnormal deviation between continuous and intermittent recording i e of Jerger s type III and IV was demonstrated in the Békésy audiometry

In *directional audiometry* only the individual analysis was performed Abnormal findings with no other explanation than diabetes was recorded in 6 cases in the oldest age group and in one in the intermediate All patients in the youngest age group had normal directional hearing (Table 3)

Correlation between Abnormal Audiological Results and Manifestations of the Diabetic Disease in the Individual

The histories were carefully evaluated and directly related to the diabetic disease *per se* Many patients demonstrated hearing loss in pure tone audiometry (Table 3) The audiograms were considered particularly in relation to noise exposure If the audiogram showed a hearing loss that could reasonably be explained by the history they are not included in the following figures Only hearing losses with no other reasonable explanation than diabetes were taken into account In speech and distorted speech audiometry as well as in the stapedius reflex measurements and Békésy audiometry

TABLE 4 *Correlation between hearing impairment and severity of diabetes*

Testing method	Abnormal audiometry due t diabetes in the 33 patients %h most diabetic complications, 11 from each ge group	Abnormal audiometry due t diabetes in the whole series, 90 patients
Pure tone audiometry	9	11
Speech audiometry	30-	31
Distorted speech audiometry	32%	40
Stapedius muscle reflex	6	8
Békésy-audiometry	27-	21
Directional adiometry	6	7-

all values outside the given limits are contained in the following figures irrespective of histories.

The results may be presented as follows

I. Age. The present investigation demonstrated that there is a significant number of diabetics exhibiting hearing abnormalities (Table 3) The risk f being more afflicted by hearing disorders increases with age. It is to be expected that the risk for the diabetic may be even greater when sensorineural loss due to aging is added.

From Table 3 it can also be seen that the number of patients demonstrating hearing impairment in two or more tests increases with age

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IV *Severity of diabetes mellitus* The clinical and audiological examinations made it possible to make an attempt at determining any associations that might exist between the severity of diabetes mellitus and any hearing disorder demonstrated

When the number of abnormal hearing tests in those 11 patients constituting of the age group most afflicted by different diabetic complications was compared to the total number of abnormal hearing tests in the whole series, no correlation could be demonstrated (Table 4) Even when turning the analysis and regarding each individual with any form of hearing impairment to evaluate if he was more afflicted by late diabetic complications, no correlations could be demonstrated.

Furthermore some of the late diabetic manifestations i.e. retin pathy and microangiopathy of the skin were graded according to severity Nor does an analysi to demonstrate any correlation between hearing disorders and th severity f angiopathy in terms of these parameters indicate any correlation Th above findings thus indicate th t no association existed between the severity of the diabetic process and hearing.

V *Late diabetic complications* In none of the three age groups nor in

individual analysis could any correlation be demonstrated between any type of hearing loss and such diabetic manifestations as angiopathy retinopathy nephropathy or neuropathy This is furthermore confirmed by 5 *patients with such a serious retinopathy that they were completely invalidated, though their hearing was normal*

DISCUSSION

It is well known that diabetes mellitus in many patients slowly leads to vascular changes manifested by PAS-positive thickening of the vascular wall Diabetic angiopathy has been demonstrated in most organs and also in the cochlea (Jorgensen Costa) Vascular changes have been demonstrated in the stria vascularis (Jorgensen 1962 Costa 1967) and in the vessels in the modiolus (Costa 1967) The vessels in these regions are of great importance for hearing One would thus expect the incidence of hearing loss to be greater in diabetics than in a corresponding non-diabetic population. The incidence of hearing loss reported has shown great variations. The present investigation confirms what som observers (Schroder 1954 Kindler 1955) have noted viz. that no significant hearing loss in pure tone audiometry could be attributed to diabetes mellitus *per se* Schroder however only applied pure tone audiometry to 10% of his cases, constituting about 30 audiograms (Table 1) Kindler presented a very big series of 8000 cases without hearing loss The method of testing is not given but pure tone audiograms have probably not been recorded in all these patients.

The relatively high incidences reported by others, whether pure tone audiograms were taken or not may have been due to inclusion in their series of diabetic patients of high age and hence afflicted by presbyacusis Further evidence of this are the investigations of Vigi (1950) and Profazio & Baravelli (1959) demonstrating an increasing incidence of hearing loss at higher ages

The present investigations set age limits at 16 and 50 years.

Furthermore the hearing of a group of diabetics must be compared with that of a corresponding normal group As the diabetics in the present series were not selected their hearing had to be compared with an unselected population This has apparently not been done previously When the present series is compared to the so-called *Wisconsin State Fair Survey* including 6000 unselected cases, the group means in pure tone audiometry lie well within the normal hearing range after correction to ISO standard threshold

The present investigation seems to be the first where pure tone audiograms were taken in fairly young diabetics and related to a corresponding non-diabetic population

The investigation demonstrates that there is no hearing loss in pure tone audiograms when considered as group means

Pure tone audiograms, however generally only give an incomplete assessment of hearing. It was the consistent aim of the present investigation to seek all hearing defects, whether central or peripheral. Hence it was necessary t adopt methods to detect retro-cochlear or "central" lesions for which the diabetic process could be held responsible. The present investigation demonstrated that in all the three age groups a definite degree of hearing loss of retro-cochlear origin could be demonstrated, i.e. in speech audi metry in Békésy audiometry and in directional audiometry.

The normal series constituting the basis for speech and distorted speech audiometry were young people with a good vocabulary and in a good test situation. The present series was of higher age and apparently ill people and thu the test situation was less good.

In consequence of this the limits based on healthy young subjects when applied on the present material compare unfa orably. Furthermore, the limits of speech and distorted speech audiometry might have been too strict i.e. a patient exhibiting a discrimination loss of 2% less than the set limit on one ear was considered abnormal. Most of the abnormal findings were close to the normal which is demonstrated by the group means, which are within the normal limits although the deviation is abnormal. Hence con clusions concerning abnormal speech discrimination tests must be drawn with great circumspection.

The stapedius reflex wa test to determine if diabetic neuropthy might affect the reflex arc and thus diminish or abolish the reflex. It was also tested to establish whether recruitment was present in cases with hearing loss. In 6 patient the stapedius reflex was elicited at a higher stimulation level than normal. This cannot be considered an abnormal number. Consequently diabetes mellitus does not seem to significantly diminish the reflex in patients with normal pure tone audiograms.

The abnormal finding in directional audiometry indicate a retro-cochlear lesion rather than a cochlear.

In the Békésy audiometry a particularly interesting observation was made i.e. that a high proportion of the diabetics had greater excursions than a corresponding non-diabetic series. This was interpreted to mean that the diabetics reacted slower than normal to differences in sound intensity. It cannot be settled whether this was due to "slow cerebration" vascular diabetic changes in the brain, unfavorable blood sugar levels during the test or to any other cause but it is considered an interesting aspect worth further investigation if the high excursions in the Békésy audi metry could be correlated t a retro-cochlear type of hearing impairment.

The results of the present investigation were moderately abnormal in these latter tests. The present series thus demon trated a small but definite degree f abnormality in speech and di torted speech audiometry as well as in Békésy nd directional udiometry pointing to a retro-cochlear rather than a cochlear lesion.

The patients were thoroughly examined from the clinical viewpoint and

diabetic complications of all kinds recorded From the clinical viewpoint each age group was representative with respect to the duration and manifestations of the disease

The present investigation further sought to correlate hearing to the diabetic state This was done both by groups and by individuals in the following respects sex, age and the diabetic parameters, duration and severity of the disease retinopathy angiopathy and neuropathy In the individual case a number of hearing disorders were demonstrated which were positively correlated to age The higher the age of the individual or group the more likely it will be to have hearing impairment.

Such factors as sex duration and severity had no apparent role in any form of interference with hearing function in these patients. In the present series the hearing was well preserved in the diabetics most afflicted by the diseases. Those patients demonstrating the most serious hearing impairment were not those in whom the diabetic state was most advanced These findings agree with some earlier ones though the literature includes many contradictory results

In contrast to previous investigations the present investigation thus discloses that hearing is comparatively well preserved in diabetics and in those cases with hearing impairment there was no correlation to the duration of severity of the diabetic disease This is surprising and interesting as in general these is a correlation between the duration of the diabetic disease and other sensory complications

The cochlea is also a very vulnerable sense organ in that it is supplied by an end artery—the labyrinthine artery Any interference with circulation in this vessel may have disastrous consequences for the hearing organ. More peripherally in the cochlea particularly at the capillary level the vasculature is rich and anastomoses are numerous. As the cochlea has numerous alternative capillary pathways for the maintenance of adequate circulation a patchy distribution of the diabetic vascular changes need not lead to marked changes in hearing The results of the hearing tests rather point to a retro-cochlear lesion The cochlea thus seems less prone to damage than brain tissue, perhaps because at the capillary level brain tissue is more susceptible than the cochlea to anoxia resulting from diabetic angiopathy

ZUSAMMENFASSUNG

Bisherige Versuche das Hörempfinden bei Diabetes durch einfache klinische Teste und bisweilen auch audiometrisch zu messen haben zu sehr widersprechenden Ergebnissen geführt. Die Frequenz der perzeptiven Gehörstörungen variiert bei verschiedenen Autoren zwischen 0 and 80% Aus diesem Grunde schien die Ermittlung dieses klinischen Problems durch Anwendung moderner audiologischer Prüfungsmethoden wünschenswert was bisher nicht durchgeführt worden war 99 verhältnismässig junge Diabetiker wurden untersucht Reinton Audiogramme war n in den untersuchten Gruppen durchschnittlich normal Mässige Gehörstörungen konnten aber manchmal festgestellt werden und zwar insbeson

dere dann, wenn die Patienten sowohl durch Sprachaudiometrie und sensibilisierte Sprachteste als auch durch Richtungsaudiometrie und Békésy-Audiometrie untersucht wurden. Alle Ergebnisse wurden unter Berücksichtigung des psychoakustischen Charakters der letztgenannten Teste kritisch ausgewertet. Ein Zusammenhang zwischen den beobachteten Gehörstörungen und der Zeitdauer oder dem ernstlichen Grad der Krankheit wurde nicht gefunden. Hörverlust kamen jedoch öfter bei alten Patienten vor. Männliche und weibliche Patienten waren gleichmässig betroffen. Die Ergebnisse und ihre Auswertung werden diskutiert.

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AIR EMBOLISM AS A COMPLICATION OF INFLATION OF THE TYMPANUM THROUGH THE EXTERNAL AUDITORY MEATUS

A Clinico-pathological Study of a Fatal Case

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A case is described f f tal air embolism resulting from tympanic in fl tion carried out through the e ternal auditory meatus for the treat ment f secretory otitis media. Th post-mortem f ndings, including the result of a histological examination of the temporal bone provide idence that th air left the tympanum through one or more small atural d fects in the tegmen-tympani and passed forwards outsid the dura to th region of th foramen lacerum medium Here it caused surgical emphysema of the peri-carotid con ecti e tissue and entered the venous system by rupturi g the thin-walled venous sinuses which are present at this point. Thereafter the air passed by way of the avernous and petrosal sinuses to the right side of the heart and so caused death.

As described in a modern text-book (Scott Brown, 1965) paracentesis followed by inflation of the tympanum through the external auditory meatus is an accepted f rm of treatment for secretory otitis *media* The danger of air embolism cannot be disregarded and Ahrén & Thulin (1965) of Goteborg have reported a fatality resulting from its occurrence The air entered the middle cranial fossa causing stripping of the *dura mater* and haemorrhage from rupture of a branch of the middle meningeal artery Widespread brain damage resulted and this was *the cause of death*

In second instance t be described in this paper a post mortem ex aminati n showed that death was due to a massive air emboli m with air filling of th right sid of th heart Histological examination of the temporal bone revealed that the air *from the* tympanum entered the venous ystem by way of the thin walled venous sinuses which surround the carotid artery in it intra petrous course

Clinical History Otological Findings and Operative Procedure

Mr A. a married man, ged 3 complained of deafness and tinnitus following heavy cold. When seen three weeks after the onset of his symp-

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The lesser superficial petrosal nerve is shown lying in the substance of this partition beneath the tympanic mucosa. As a result of the inflationary pressure the partition has been displaced without rupture toward the carotid canal with angulation of the nerve at the point indicated by the arrow. Gross irregular distension is also shown of the pericarotid venous spaces with much extravasation of blood into the pericarotid connective tissue. See also Figs. 4 and 5.

FIG. 2. Subject B. Photomicrograph (X4) showing normal anatomy of the carotid canal and tympanic cavity. The intervening septum of bone with numerous venous sinuses in the pericarotid connective tissue.

FIG. 3. Subject B. Photomicrograph (X40). The enclosed area in Fig. 2 at higher magnification showing the pericarotid connective tissue and thin-walled venous sinuses.

toms it was noted that the left tympanic membrane had a yellowish tinge but no fluid level was observed The right tympanic membrane was normal in appearance Conductive deafness was present and equal in the two ears 5–10 dB for the lower frequencies 40 dB for the higher frequencies. Eustachian catheterisation and inflation were performed with ease with immediate subjective improvement of hearing Following this procedure no fluid level was seen in either tympanum Thereafter and on nine occasions Eustachian inflation was performed over a period of 6 weeks. Following the 5th inflation a fluid level was seen in the left tympanum The tinnitus in the right ear quickly improved and the hearing returned to normal In the left ear however the tinnitus and deafness continued After the 9th inflation no treatment was given for a period of one month The fluid level in the left tympanum was then found to be unchanged with persistence of tinnitus and deafness Treatment by means of paracentesis was then proposed under local or general anaesthesia The latter was preferred by the patient Anaesthesia was induced by means of an intravenous injection of thiopentone and continued with nitrous oxide oxygen and trilene using a facemask The left tympanic membrane was incised in the lower posterior quadrant and a little thin fluid sucked out There was no bleeding A small nozzle attached to a small rubber Politzer bag was held in the external auditory meatus and an assistant squeezed the bag There was considerable resistance at first but this was overcome and air was heard to issue from the Eustachian tube After several such inflations the procedure was terminated and the anaesthetic discontinued The drapes were then removed and at this moment 2–3 minutes after the stopping of the anaesthetic respiration ceased The thorax and face were cyanosed and the pulse absent The pupils rapidly dilated and despite energetic resuscitation the patient could not be revived No exact value can be given for the air pressure exerted in the external auditory meatus. With air tight joints and strong manual compression of the bag a peak pressure of 760 mm of Hg (1 1 kg/cm^2) was found to be attainable However as used at the operation, the system was not air tight and the air pressure must have been considerably lower Necropsy was carried out 6 hours after death

Post mortem Findings

In view of the likelihood of an air embolus the heart and great vessels were first examined *in situ* under water There was a great deal of air in the right ventricle and pulmonary artery which caused the heart to float The heart was otherwise normal and there was no blood clot embolism of the pulmonary vessels The lungs showed patchy collapse and some oedema

FIG. 1 Subject L. Photomicrograph (X4) h w i g the tympanic cavity nd c rotid c n l Le l 1.073 mm bel w highest point of ca l t it g on. In the pl ce f the lo r sept m which n small separates these compartments a connective tissu partition f present.



FIG. 4. Subject A. Phot micrograph (X4). Tympanic ca ity nd carotid canal. Lev l 0.373 mm below highest point of canal nd abov the rtery itself. The pericarotid enous si ses are distended nd empty f blood cells. There i much extra asation of blood i t the peric rotid connecti tissue.

FIG. 5. Subject A. Photomicrograph (X4). Tympa ic ca ity nd carotid canal. Lev l 3.125 mm below highest point f canal. The pericarotid enou sinuses are grossly distended nd empty f blood cells. The connecti tissue is disorganised nd reduced t irregula broken-up trabecul.

FIG. 6. S bject A. Carotid canal. Lev l 6.4 mm below it highest point. The pericarotid nd connecti tissu and enou paces re normal.

FIG. 7. Sk ll base of normal subject. The carotid rtery has emerged pon the upper surface f the temporal bone rather rly in its forward course t the foramen lacerum med m. A mall hole, indicated by the rrow has been drilled i the tegmen tympani It dist nce from the point of emergence of the carotid artery i 10 mm.

ject are revealed in the horizontal secti n shown in Figs. 4 and 5, at levels of 0.37 and 3.125 mm respecti ely below the highest point of the canal at it genu. A shown in Fig. 1 similar changes in the pericarotid tissues

but were otherwise normal Apart from congestion the liver spleen and other abdominal organs were normal The skull brain and meninges were normal No elevation was noted of the dura mater from the surface of the temporal bone, which was removed for histological examination and fixed in 10% formol saline

Histological Examination of the Left Temporal Bone

The bone was received at the Otological Research Unit of the Medical Research Council National Hospital Queen Square, London on 21 0 64 The dura mater had been removed from its posterior and upper surfaces. No defects were noted of the tegmen tympani The bone was decalcified in 8 N buffered formic acid and embedded in celloidin Serial sections in the horizontal plane were cut at 25 μ and every tenth section stained for examination with Ehrlich s haematoxylin and a mixture of eosin and Biebrich scarlet

External auditory meatus Normal

Tympanic membrane Normal apart from a posterior linear defect resulting from the myringotomy

Tympanic cavity Scattered collections of pink staining fluid were present evidently the remnants of the fluid effusion Anteriorly there was an extensive dehiscence of the bony septum between the tympanic cavity and the carotid canal the gap being filled by a thin partition of tympanic mucosa and connective tissue In Fig 1 this partition is shown displaced medially with angulation of the lesser superficial petrosal nerve contained in its substance The appearance is in accord with an elevation of intratympanic pressure At no point however does the partition show any break of continuity so excluding the possibility that it provided an exit pathway for the air from the middle ear

Cochlea Endolymphatic and perilymphatic spaces normal Reissner s membrane, organ of Corti stria vascularis, spiral ganglion and cochlear nerve fibres normal

Vestibule saccule utricle and semi-circular canals Membranous walls and neurosensory apparatus of maculae and cristae normal Ductus and saccus endolymphaticus normal

Carotid canal Severe pathological changes were found to be present in the venous sinuses which are normally present in the connective tissue network which here surround the carotid artery The nature of the changes is clarified by comparison with the findings in a normal subject These are shown in Figs 2 and 3 The connective tissue is delicate and the venous sinuses appear as thin walled blood-containing spaces Anteriorly they drain into the cavernous sinuses Anteriorly too is the area of the foramen lacerum medium which adjoins the cavum Meckelii here the contents of the carotid canal are overlaid by and in direct contact with the dura mater

The changes in the carotid canal of the left temporal bone of our sub-





Fig. 4. Subject A. Photomicrograph (X4). Tympa ic ca ity nd carotid ca l. Lev l 0.575 mm below highest point of canal nd abov the rtery itself. The perica tid enous sinuses re distended nd empty of blood cells. There is much extravasation of blood int the pericarotid connectiv tissue

Fig. 5. S bject A. Photomicrograph (X4). Tympanic cavity nd carotid canal. Lev l 5.125 mm below highest point of canal. The pericarotid enous sinuses are greatly distended and empty of blood cells. The connecti tissue is disorganized nd reduced to irregular broken-up trabec lae

Fig. 6. Subject A. Carotid ca l. Level 6.4 mm below its highest point. The pericarotid nd connecti tissu and enous paces are normal.

Fig. 7. Skull base of normal subject. The carotid artery has emerged po the pper surface of the temporal bone rather early in it forw rd course t the foramen lacerum medium. A small hole, indicated by the rrow ha been drilled in the tegmen tympani. It distance from the point of emergence of the carotid artery is 10 mm.

ject are revealed in th horizontal section shown in Figs. 4 and 5 at lev ls of 0.575 and 5.125 mm respectively below the highest point of the canal at its genu As shown in Fig. 1 similar changes in the pericarotid tissues

were present at an intermediate level (1 075 mm below the highest point of the carotid canal) In Fig 4 is shown the dehiscence already referred to in the bony carotico tympanic septum The *venous sinuses are distended* and largely empty The connective tissue net work is distorted and contains much blood in its interstices. In Fig 5 similar changes, more severe in degree are shown Anteriorly the venous spaces are grossly distended and practically emptied of blood cells. The connective tissue separating the venous spaces is reduced to irregular trabeculae which in many places appear to have been ruptured In Fig 6 is shown the carotid canal in the lower part of the vertical portion of its course The pericarotid connective tissue and venous spaces are here normal

DISCUSSION

It is appropriate to compare the clinico-pathological data which have now been presented with those relating to the somewhat similar case reported by Ahrén & Thulin to which an earlier reference has been made In both the primary mishap was the *eruption of air from the tympanum* into the tissues Ahrén & Thulin were able to show that in their patient the air left *the tympanum through certain natural bony defects in the tegmen tympani* There was extensive stripping of the middle fossa dura from the bone with rupture of a branch of the middle meningeal artery A massive extra dural haematoma resulted the brain was displaced and damaged and this was the cause of death The heart was hypertrophied but otherwise normal The lungs showed bronchopneumonia No evidence of air embolism was found The temporal bone was not histologically examined

In the present case events pursued a rather different course The air from the tympanum somehow penetrated into the pericarotid connective tissue and then tore and entered the thin walled venous sinuses which are contained therein By these it was carried into the cavernous sinuses and so made its way into and filled the right side of the heart So much seems certain It remains however to identify the pathway followed by the air from the tympanum to the carotid canal The most direct route would certainly have been through the dehiscence found to be present in the bony carotico-tympanic septum However the histological findings show clearly that although the connective tissue partition which was found to occupy the gap had been displaced by the inflationary pressure no rupture had occurred As an alternative, and indeed the only possible alternative we are led to infer that as in Ahrén & Thulin s case the air left the tympanum through one or more small hiatuses in the bony tegmen which as anatomical anomalies are by no means very rare Furthermore they may be small enough to escape notice on macroscopic examination of the bone as was the case in this instance. Thereafter the conclusion would seem inescapable that the air passed directly forward beneath the dura to the roof of the carotid canal in the region of the foramen lacerum

medium. In this its passage must have been favoured by certain anatomical features which were found to be present. Thus, the carotid artery lay at a high level within the temporal bone and emerged from its upper surface early on its forward course This amounting to a backwards extension of the foramen lacerum medium, would clearly provide a short and low resistance pathway for the passage of air between a tegmental hiatus and the peri-carotid connective tissue This is illustrated in Fig 7

ZUSAMMENFASSUNG

Ein Fall vo tödlicher Luftembolie erursacht durch eine Luftdusche die om u seren Gehörgang aus zur Behandlung einer serösen Mitt lohrentzünd g ausgef hrt wurd wird beschrieben Die utoptischen Befunde und die zusätz lichen Resultat der hi t l gischen U tersuchung der Schläfenbeine la sen er ken n, da di Luft die Pauke höhle durch inen oder mehrere klein n för liche Defekt im Tegmen t mpani verliess d ausserhalb der Dura nach m in di Gegend des F ramen lacerum medi m wanderte An dieser St lle bewirkte si in hirurgisches Emphysem des die Caroti umgebenden Bind gew bes und indem sie di hier vorhande en dünnwandigen venösen Sinuse durchbra h gelangt sie in das venöse System. A schliessend wa derte di Luft über Sinus cavernosus u d Sin s petrosu in die recht Herzhälfte und fuhrt so um Tod

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DESCRIPTION OF THE SD 1 HIGH SPEED AXIAL ROTATION DEVICE

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A high speed axial rotation device capable of carrying animal subjects, the SD 1 was constructed and evaluated for vestibular research at the University of Iowa The device can be controlled automatically by using a Data Trak curve-follower programmer or manually if desired The drive system for the device is a Schaevitz GSD2PR variable-speed motor with associated electronic components, including a solid state power supply with excellent voltage regulation capability The rotating module is dynamically balanced to insure maximum performance and personal safety Above 50 degrees/sec angular velocity of the device increases linearly with increases in setting of the speed-control potentiometer Control of angular velocity can be maintained constant ±0.20% for any specific setting of the speed-control potentiometer Control of angular acceleration and deceleration is excellent over the range from 1 degree/sec² to 3 10 degrees/sec² By utilizing either the programmer or plugging unit angular accelerations and decelerations of constant linearity can be obtained The SD 1 provides a sufficient range of angular velocities and angular accelerations for conducting a variety of experiments in vestibular research it is particularly suited for providing the maximal and supramaximal levels of stimulation necessary for the efficient pro-*duction of vestibular suppression*

Vestibular research at the present time places certain unfortunate constraints upon the investigator one of these is that he has only two effective means of stimulating the semicircular ducts—caloric stimulation and angular acceleration of the whole organism A very great proportion of vestibular research has involved threshold stimulation of the semicircular ducts, utilizing angular accelerations of 1×10^{-1} to 1×10^{1} degrees/sec² There is additional knowledge to be obtained however from the use of maximal and supramaximal stimulation Such levels are to and beyond the point of overload of the vestibulo-ocular reflex It has been demonstrated that such stimulation levels, many times in excess of threshold produce physiologic responses without end-organ damage (McCabe & Gillingham 1964) A special device the SD 1 has been developed for use in the exploration of those areas where the stimuli are far in excess of threshold

The SD-1 is a high speed heavy-duty axial rotation device (Fig 1) de-

signed for producing and investigating vestibular suppression (habituation) It is capable of continuous rotation in the horizontal plane with a maximum angular acceleration of 8.3 revolutions/sec² (rps²) and a maximum angular velocity of 8.3 rps. The device can be operated either automatically or manually

The SD 1 is of twofold value t vestibular research (1) it can produce vestibular suppression in animals to the maximum degree and in minimum time by irtue of the fact that the high angular accelerations of which the SD 1 is capable can provide a high level of energy transfer to the cupula-endolymph system (2) because of its unique control system, the SD-1 can also be used in experiments requiring prolonged low level angular accelerations.

Mechanical Features

Two integral units constitute the SD 1 high-speed axial rotation device the test stand and the operator's control console

The test stand is a fabricated steel weldment with front, rear and side panels removable for access to the drive and slip-ring components. The test stand contains a 3-hp, shunt wound, d.c. motor with heavy-duty cogged belting, tach generator digital tachometer slip-ring assembly and the animal mounting fixture The test stand is 72 in. high, 52 in wide, and 24 in deep

The operator s control console is fitted with casters so that it may readily be moved from one position to another within a 25-ft. radius of the test stand It contains the following equipment, whi h provides for the compl te control of the test stand

1 Manual control panel
2. Solid-state electronic drive system
3 Curve-f llower programmer
4 Electronic counter

The control console stands 60 in high, 44 in. wide and 22 in. deep

The high-speed rotating assembly is dynamically balanced so that maximum performance and safety are insured In the rotating assembly a tooth bar restraint is utilized after the manner of Henriksson (Henriksson *et al* 1961) so that all the forces applied to the animal are delivered by that module and none by the animal The experimental animal is constrained in the center of the rotating assembly by a bivalved form-fitting mold of Lockfoam

Electrical Features

Slip rings are provided for the transfer of information between the rotating experimental animal and th monitoring equipment There are twelve bronze rings, each faced with 1/16-in. coin silver The brushes which contact the rings are composed of a special silver-graphite combination

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Fig. 2. Slip-ring noise level as [illegible] function of angular velocity (rps) of the SD-1. The [illegible] period [illegible] record was made immediately after [illegible] rps² acceleration [illegible] terminal [illegible] of [illegible] rps. The signal-to-noise ratio is 10 to 1.

Fig. 3. Schematic of the drive system.



FIG. 1 The SD-1 high-speed axial rotation device

which has been found to result in the proper wear relationship between ring and brush and to permit operation with a minimum of extraneous noise (Fig 2) Three brushes are provided per ring to maintain uniform contact

The drive system (Schaevitz GSD2PR) (Fig 3) incorporates a tachometer feedback-controlled circuit for supplying armature and field current to a stabilized shunt wound d c motor This drive will provide a wide range of motor speeds with precise speed settings with high torque available at any set spreed An important characteristic of the GSD2PR is the high torque (plugging) response to sudden reduction in speed setting at any speed level The usefulness of the drive system is enhanced by several special features

1 Tachometer feedback control system
2 A reversing system to change direction of motor rotation
3 Automatic utilization of the full limit value current until the stabilized speed setting is closely approached, thus providing maximum acceleration of high inertia loads
4 Availability of high torque plugging to a dead stop for maximum deceleration
5 Push-button starting at any speed setting
6 Push button stopping by dynamic braking

The SD 1 can be controlled automatically by using the model FGE-5110 Data-Trak curve follower programmer The speed of the rotating module

TABLE 1 *SD-1 angular velocity at 10 different positions of speed-control potentiometer*

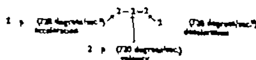
Position of speed-control potentiometer	Clockwise angular velocity degrees/sec	Counter clockwise angular velocity degrees/sec	Position of speed-control potentiometer	Clockwise angular velocity rps	Counter clockwise angular velocity rps
20	0	0	100	0.712	0.715
25	22.506	22.795	125	1 000	1.005
30	40.192	40.792	200	1.550	1.553
35	56 559	56.969	300	2.392	2.393
40	72.585	72.645	400	3.235	3 233
50	103.779	103.779	500	4.067	4.070
60	131.373	131.673	600	4 900	4.903
70	161.367	161 966	700	5.737	5.733
80	193.561	195 987	800	6.568	6.572
90	226.155	226.455	900	7 405	7 404
100	254.740	254.996			

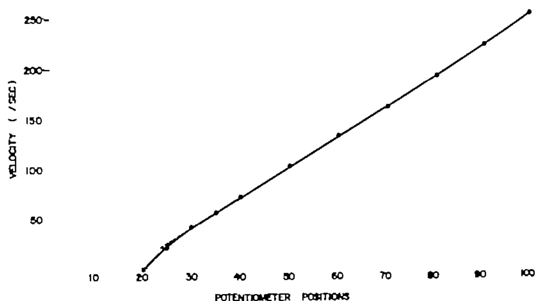
is indicated in revolutions per second on a five-digit electronic counter (Hewlett-Packard Model 521CR)

Performance Data

Two methods were used to obtain performance records of the SD-1 axial rotation device (1) continuous records of velocity and acceleration were recorded by means of a d.c. tach generator feeding into a d.c. amplifier (Sanborn Model 1 0-1600) and direct writer (2) a signal received from an angular velocity pickup driven by the main spindle through a belt and sprocket was delivered to the electronic counter The data from each source were taken for each of 20 settings of the speed-control potentiometer At each speed setting, the SD-1 was driven 20 times, alternately clockwise and counterclockwise without resetting the speed-control potentiometer The response of the system is seen to be extremely linear (Fig. 4 and Table 1) a result t be expected from such a velocity-controlled servo system

A somewhat different procedure was used to determine the reliability of the SD-1 system in reproducing acceleration and velocity when the dri e wa controlled by the automatic programmer Ten different programs (Table 2) were used in these determinations. Note that the first digit in the program represents angular acceleration in rps^2 the second digit represent angular velocity in rps, and the third digit represents deceleration in rps^2 so that





8
7
6
5
4
3
2
1
VELOCITY (RPS)
100
200
300
400
500
600
700
800
900
1000
POTENTIOMETER POSITIONS

FIG 4 V locit 20 diff rent po iti n f peed-co trol pot ti m t



FIG. 5 A program sample showing acceleration-velocity-deceleration profil of lock wise 4-4-4 and counterclockwise 4-4-4 rotation.

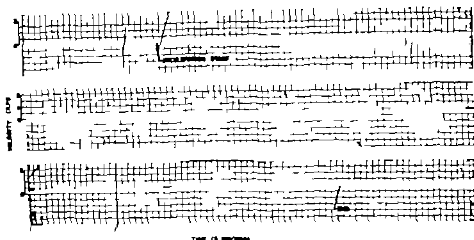


FIG. 6. A typical example of data showing the li eality of acceleration of 1 degree sec²



FIG. 7 Profile of 4-4-4 program of accelerations nd decelerations with the use f the pl gging k Compare ith Fig. 5.

Beze ch ung SD-1) konstruiert und angewa dt. Die Apparatur k n sow hl utomatisch mit Hilf el es D ta-Trak Kurven npassungsgerates wie auch rein manuell gesteuert werden Die Anord ung wird durch inen Schaevitz-G5D2PR-Motor mit lektronisch seh genau regulierbarer Umlaufsgeschwindigkeit nge trieben Der rotierend T il der Apparatur ist dynamisch usbalanciert um ma imale \ tabark it und Si herh it der Anord ng zu gewährleisten. Die Win k lgeschw i digk it der Anordnung nimmt oberhalb von 50 /sec linear zu mit der Einst llung des Potentiometers für die Geschwindigkeitskontrolle Bei fester Einstellung des Potentiometers kan die Wink lgeschwindigk it innerhalb einer Ma

TABLE 2

Program number	Program
1	1 1 1
2	1 2 ?
3	1 3-3
4	1 4-4
5	1 5-5
6	1-6-6
7	1
8	2 2 2
9	3-3-3
10	4-4-4

Figure 5 represents the typical profile of an automatically controlled 4-4-4 clockwise, 4-4-4 counterclockwise program Figure 6 shows an example of a slow acceleration It was calculated that the obtained profiles of acceleration and velocity were within ±2% of the programmed values, even at the points of maximum change of acceleration

The data presented herein were obtained over a period of two weeks of testing and evaluation of the SD 1 The solid state power supply for the device provided exceptionally constant, accurate voltage regulation and as a result of this, over all performance was very satisfactory

As shown in Fig 4 angular velocities obtained on the SD 1 are a linear function of the setting of the speed-control potentiometer providing the velocity is 50 degrees/sec or more The velocity at a given setting will be constant and reproducible, under those circumstances within ±0.2% in both directions. Below 50 degrees/sec the relationship between obtained velocity and potentiometer setting becomes nonlinear and the reproducibility diminishes to ±3% at a given setting Using the direct writer system we were unable to detect any deviations from set angular velocity the reproducibility values of ±0.2% and ±3% were obtained through the use of the electronic counter

Ramp-function angular accelerations and decelerations were obtained both by using the curve-follower programmer and by using the plugging unit In all cases the accelerations and decelerations were constant throughout their periods within ±2% (Figs 5 and 7) The SD 1 is capable of delivering uniform angular accelerations over a range from 1 0 degree/sec^2 to 3 0 × 10^3 degrees/sec^2 Such a range includes the maximal and supramaximal stimuli in terms of vestibular end-organ response so that the upper limit of this organ's functional capability is easily reached

ZUSAMMENFASSUNG

Für Vestibularuntersuchungen an Versuchstieren wurde für die Universität in Iowa eine Spezialapparatur fur hohe axiale Rotationsgeschwindigkeiten (mit der

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CORTICAL RESPONSES TO ROTATION

I. Responses Recorded after Cessation of Rotation

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Averaged cortical responses to labyrinthine stimulation induced by sudden cessation of single rotations were studied using a Mnemotron Computer of Average Transients. Following rotation there appeared in cats with the eyelids closed diffuse slow, sometimes multiphasic responses. They were probably due to excitation of the diffuse thalamic system. In human subjects similar responses could be obtained either diffusely or prevalent or exclusively from the precccipital and/or parasagittal area. The responses observed in posterior parts of the cerebral hemisphere following cessation of rotation appeared also if the animals were flaccidized, or the second somatic sensory area was ablated in both hemispheres. Bilateral labyrinthectomy abolished these responses. While the observation of the ocular reaction to labyrinthine stimulation permits one to ascertain the excitability of the vestibulo-ocular reflex arc only, the recording of the cortical responses to rotation may perhaps be developed into a clinical tool for the study of the state of corticopetal systems carrying labyrinthine impulses.

For a study of the cortical responses evoked by stimulation of the *non-acoustic* part of the inner ear production of an adequate stimulus, i.e. an endolymph flow, seems preferable to electric stimulation, since the latter may easily affect adjacent structures (*nervus cochlearis, nervus intermedius*). Furthermore direct electric stimulation of the *labyrinth*, of the vestibular nerve or its branches, *as a rule* is possible in animal *experimentation* only. The usual type of stimulation by 10 rotations in 20 sec on a Bárány chair, however, is too intense for a study of possible localized cortical responses, because the excitation quickly affects the whole cortex. It was, therefore, attempted to use single *rotations* only. By *employing* an averaging Mnemotron computer the responses in constant time relationship to the stimulus (cessation or onset of the rotation) could be summed and the discharges unrelated to the stimulus diminished. It was hoped that by using rotation as the stimulus a method could be developed that could also be applied to clinical testing.

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ginale von ±0,2% konstant gehalten werden Ebenso kann die Winkelbeschleunigung, und zwar sowohl bei Akzeleration wie bei Retardation innerhalb des Bereiches von 1 /sec² bis 3×10 /sec² mit sehr guter Genauigkeit eingestellt werden, sowohl manuell wie mit dem Kurvenanpassungsgerät Der SD 1 ermöglicht somit eine hinreichende Spanne von Einstellungsmöglichkeiten der Winkelgeschwindigkeit und Winkelbeschleunigung für die variierenden experimentellen Anforderungen bei Vestibularuntersuchungen Im besonderen können mit ihm auch die Maximal bzw Supermaximal Stimulationsniveaus erreicht werden, die notwendig sind um auch den Bereich der Vestibular Suppression in die Untersuchungen einbeziehen zu können

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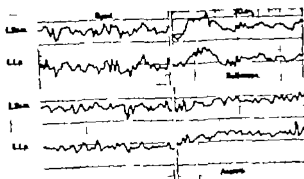


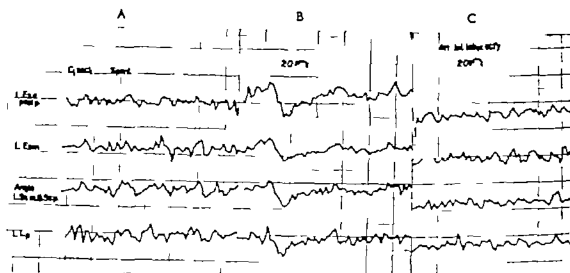
FIG. 2. A eraged ponta eou dscharges nd responses following 20 single cou terclock wise rotations. Upper 2 record cat i bulbocapni (25 mg/kg) cat lepsy Lower 2 record same cat under sodium pentobarbital anesthesia. *L. Ss. m.*, Left gyru pra syl i medius; *L. Lp*, left gyrus lateralis posterior

direction, the response was transmitted to the computer system after the recording the chair was slowly returned to the starting position in order to avoid excessive twisting of the connecting wires. After a pause of 1 minute the rotation was repeated, and the responses following 10 to 30 or more single rotations were averaged by the computer In this apparatus the averaging is synchronized by the stimuli so that responses related to the stimuli are reinforced, while the electric activity not relater to the stimuli is n t synchronized and becomes reduced After each series of ten rotations the averaged response was displayed on a X Y plotter (Electro Instru ments Inc. Model 500) so that not only the effect of the summation but also possible changes in the excitability of the labyrinth and/or of its centers, e.g habituati n effects could be observed The reactions following rotation in the opposite direction e.g counter-clockwise were studied at a later period on the same day sometimes on another day The deceleration was not measured and can be estimated only For 1 rotation/3 sec there would be a deceleration of 120 /sec assuming it would take 1 sec to attain a complete stop Since the cessation of the rotation probably took place within a shorter period, the above value should be considered a minimum

RESULTS

Following rotation in cats, slow sometimes multiphasic responses can be elicited not only from the region of the gyrus ectosylvius anterior and gyrus suprasylviu anterior but also from the posterior parts of the hemisphere f om the posterior and middle ecto- and suprasylvian and lateral gyri (Fig. 1) The peak latencies were rather long, above 0.3–0.5 sec.[1] These

[1] The exact time interv l bet ee the cessation of the rotation and the triggering of the computer w not measured.



F g 1 Cat Transverse secti n of cord at C_1 Compare averaged ponta eou discharges f cortex (A) 20 averaged postrotat ry responses bef re (B) and afte (C) bilat ral lab rinthectomy *L Es a post p* Left gyrus ectosyl ius anteri r posteri r part *L. Es. m* l ft gyrus ecto ylvius medin *L. Ss m* l ft gyrus suprasylvius medius *Ss p* gyrus suprasylvius post rior *L. Lp* l ft gyrus lateralis post rior Time signal in Figs. 1 t 8 0 4 ec.

Preliminary reports were presented at various congresses (1965) Subsequently *Greiner et al (1967) also* used an averaging computer and were able to isolate in the electroencephalogram slow evoked potentials on symmetric" stimulation of the labyrinths (clockwise rotation followed by counterclockwise rotation) or on "asymmertic stimulation (rotation in one direction only)

MATERIAL AND METHOD

The experiments were performed on 37 cats and 43 awake human subjects without organic, neurological or labyrinthine disorders The cats were maintained in bulbocapnine catalepsy In some instances the effect of addi tional pentobarbital anesthesia was ascertained In the human subjects *Grass scalp electrodes were used In cats the electrodes (stainless steel balls,* diameter 1.2–1.3 mm soldered to Teflon coated silver wire) were placed epidurally through a small drill hole in the skull and kept in place by fixing the connecting wire in the drill hole by a plastic plug Mostly the recording was unipolar In cats the head holder or an electrode placed on the frontal *sinus, in human subjects an electrode attached to the chin served* as the reference electrode In some instances also bipolar derivations were used During these experiments, the eye lids of the experimental animals or human subjects were kept closed in order to prevent optokinetic responses The wires connecting the cerebral or scalp electrodes with the recording system were conducted *in the axis of the rotating chair* over the head of the tested subject The average duration of each rotation was 3 seconds As soon as possible following each rotation e g., in clockwise

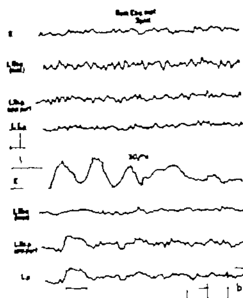


Fig. 5. Comparison of electronystagmogram (*E*) and cortical postrotatory responses in cat with gyrus ecto- suprasylvius anterior bilaterally extirpated. Cat in bulbocapnine catalepsy. *a*, Records in resting state (averaged); *b* records after 10 clockwise rotations (averaged). *L. Es. a.*, Area of extirpation of left gyrus ectosylvius and suprasylvius anterior. *L. Ss. p.*, left gyrus suprasylvius posterior; *L. Lp.* left gyrus lateralis, posterior part.

spinal segments nor immobilization by gallamine triethiodide (Flaxedil) prevented these reactions. They could no longer be elicited after bilateral elimination of the labyrinth by injection of 70% alcohol or 4% formalin into the round window (Fig. 1). The results did not differ whether the noise from an adjacent room was excluded or not, so that acoustic stimuli

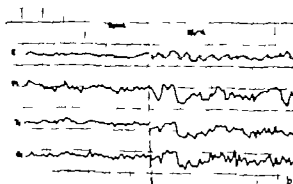


Fig. 6. Human subject without organic disease. Averaged electronystagmograms (*E*) and monopolar EEG (scalp) records. *a*, Before rotations; *b* after 15 single clockwise rotations (averaged). Similar responses in the frontal (*F*) temporal (*T*) and occipital (O_1) leads.



Fig 3 Cat Bilateral destructi n of gyrus ecto yl ius anterior and gyrus suprasylvi anterior

reactions were rather sensitive to anaesthesia pentothal anaesthesia diminished or abolished them (Fig 2)

In order to ascertain whether the responses in the posterior part of the hemisphere were due to a propagation or spread from the region of the gyrus ectosylvius anterior and gyrus suprasylvius anterior which some regard as the vestibular cortex this area was extirpated uni or bilaterally These ablations did not prevent the appearance of the responses in the posterior part of the hemisphere (Figs 3 and 4)

In order to analyze the origin of these responses, transverse sections of the cord at the first cervical segment were performed (Fig 1) Neither such transverse sections interrupting the ascending impulses from the

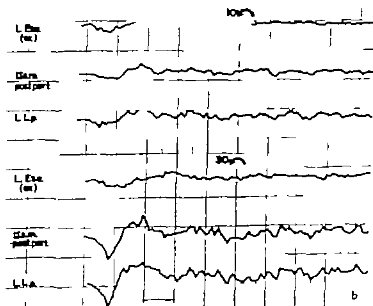


Fig 4 A raged po trot t rt cal respo ses I cat k pt cat I ptic t t b bulbo-pain (brain b wn in F g 3) l ft gyru ectosyl I t I d pra yl I teri bl ted a Effect f 10 I gl u t relockwise rot tl b ffect f 30 I gl co t lockwise rot ti ns. *L Es a* Are f bl tl f left gyru ectos l l terior *L Ss m* l ft gy u pr l iu m diu *L Lp* l ft gyru l terall posteri

DISCUSSION

Apparently one deals with so-called secondary evoked responses. The long peak latency and sensitivity to anaesthesia suggest a polysynaptic afferent pathway. Since fibers from the vestibular nuclei to the reticular formation (Obersteiner, 1912) and reticulo-thalamic connections (Held, 1923; Godlowski, 1936) are known for a long time it may be assumed that the vestibular impulses reach the diffuse thalamic projection system. There exist, however, certain local differences of the reaction particularly in man, in that these reactions were often more pronounced and/or longer lasting in the posterior part of the hemisphere in the vicinity of the visual cortex, than in anterior parts (Fig. 6). It would seem that those parts of the diffuse thalamic projection system are particularly stimulated by the vestibular impulses that project to the vicinity of the visual cortex. The role of the pulvinar in this conduction requires further study. In this connection it may be recalled that Moruzzi (1954) pointed out for the reticular activating system that sensory stimuli of low intensity may activate part of this system, while on intense and abrupt stimulation a massive discharge of the reticular neurons is likely to occur. For the preoccipital responses observed in man the possibility also should not be neglected that they may be due to impulses propagated from the second somatic sensory area that is supposed to lie in the human in or around the upper bank of the sylvian fissure (Locke, 1962).

ACKNOWLEDGMENT

The technical assistance of Mr. A. Robbins in the first part of these studies and the advice of Dr. G. R. Stewart, Mr. G. V. Jacoby and Mr. Ch. Zanes regarding physical problems are acknowledged.

ZUSAMMENFASSUNG

Die Rindenreaktionen auf Labyrinthreizung durch plötzliches Anhalten von Einzeldrehungen wurden mittels eines Mnemotron-Computers summiert. Nach Rotation erschienen bei Katzen mit geschlossenen Lidern diffuse langsame manchmal multiphasische Reaktionen. Dieselben waren wahrscheinlich Folge der Erregung des diffusen thalamischen *Projektionssystems*. Beim Menschen konnten ähnliche Reaktionen erhalten werden, entweder diffus oder vorwiegend oder ausschliesslich in der Area *praeoccipitalis und/oder der Area parastriata. Die* Reaktionen, die in hinteren Teilen der Hemisphären nach Bremsung der Drehung beobachtet wurden, erschienen *auch nach Lähmung mit Flaxedil oder beiderseitiger* Ausschaltung der zweiten somatischen sensorischen *Region. Beiderseitige* Labyrinthausschaltung beseitigte *diese Reaktionen. Während die Beobachtung* [illegible] Augenreaktionen bei Labyrinthreizung *nur die Erregbarkeit des* [illegible]

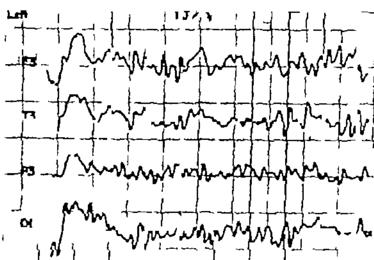


Fig 7 Human subject without organic disease Postrotat ry responses to 10 singl clockwise rotati ns (averaged) F_s, Frontal T_s, temporal P_s, parietal O_s, occipital leads. Response in O prolonged and with higher amplitude than in othe leads.

of low intensity did not seem to change the results The cortical responses were independent of the postrotatory nystagmus (Fig 5)

In man either diffuse responses or responses limited to or prevalent in the preoccipital (area 19) and/or the parastriate region (area 18) were noted (Figs 6–8) These reactions also showed long latencies and were sometimes multiphasic in character In parts of these studies, electronystagmograms, in others electromyograms of the neck muscles were simultaneously recorded An interference of corneo-retinal or neck muscle potentials occurred only rarely and such cases were not considered useful for valid conclusions. In the great majority of the records this factor played no role and a cerebral origin of the potential discharges must be assumed

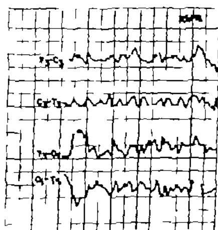


Fig. 8 Hum n subject without g nic disease Bipolar scalp EEG with phase reversal in O Averaged post otat ry responses to 10 i gl lockwi rot ti s. F_s, Front l C_s, central T_s, temporal O_s, occip t l leads.

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A COMPARISON OF AUDITORY AND VESTIBULAR RESPONSES IN HEARING-IMPAIRED CHILDREN

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Montreal Quebe Canada

Bone and air conduction thresholds f a group of twenty-five severely heari g-impaired children were measured and compared with the results of calo ic tests f vestibular function recorded by electronystagmography Although in general the presence of a vestibular response is related to measurable bone cond ction responses, but not to air conduc tion thresholds, and the absence of a vestibular response is related to severe air conduction hearing loss but ot to bone conduction thresh lds, the relatio ship between auditory and vestibular responses i of n gligible value in predicting hearing thresholds from vestibular re sponses in individual cases. Neither the vestibular hearing theory or the tactile hearing theory lone can explain the occurre e f a low frequency ir-bon gap in all cases.

Sensorineural type hearing loss is characterized by bone and air conduc tion thresholds which are essentially the same Conductive-type loss, *on the other hand* is characterized by bone thresholds which *are at least 10 dB* better than air thresholds, i.e there is an air bone gap There are, however possible exceptions to the above statements. *Often in* instances of severe hearing loss, low *frequency bone thresholds* are more sensitive than air thresholds. This finding which theoretically indicates a *conductive-type* loss generally occurs in contradiction to a medical diagnosis of sensorineural impairment. *Bocca & Perani (1960)* hav observed *that* "this peculiar be haviour of bone conduction only concerns the *frequencies* between 125 and 500 c/s" They also observed that these thresholds are rarely better than 20 to 30 dB hearing level They explained these results in terms of a vestibular hearing mechanism. *Nober (1964) has* observed similar findings, but suggested that low frequency bone thresholds *reflect tactile* exterocep tion.

The controversy over vestibular *versus tactile* hearing has clinical sig nificance relating to the *integrity of the* vestibular mechanism, because Bocca & Perani (1960) have *suggested* that the absence of bone responses i dicates an impaired vestibular mechani m. It is also important because

This research was partially supported by Grant MA 1652 from the Medical Research Council of Canada t Dr Don ld G Doehri g.

Reflexbogens zu prüfen gestattet könnte Registrierung der Rindenreaktionen auf Drehung vielleicht in eine klinische Methode zum Studium des Zustandes der Systeme ausgebaut werden die labyrinthäre Impulse zur Rinde leiten

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Electronystagmography

The procedure used is essentially that described by Fitzgerald & Hallpike (1942) except that eye movements are recorded electrically and the eyes were kept closed during caloric testing. The silver disc electrodes were positioned one immediately lateral to each eye to record the horizontal nystagmus, and one above and below the left eye to record the vertical nystagmus. A ground electrode was positioned in the centre of the forehead.

Caloric test procedure

Irrigations were carried out with the patient in the supine position head inclined 30° above the horizontal. The irrigations were carried out at 10-minute intervals. During irrigation the child was asked to count or was questioned verbally in order to maintain a constant state of arousal. If a response was obtained the test was considered complete. In those cases where a response was not obtained, the test was repeated at a later date. At the second test 25 cc of ice water was used in each ear. If no response was elicited by this test it was considered that the child had absent vestibular responses. It is important to realize that the vestibular response was not recorded as absent until every known procedure had been tried in an effort to elicit a response. It should also be noted that this test gives no information about the condition of the utricle and saccule.

RESULTS AND DISCUSSION

The results of this study are presented and discussed under headings corresponding to the questions posed in the introduction.

The Incidence of a Pronounced Low Frequency Air-bone Gap

In order to determine the incidence of a pronounced low frequency air-bone gap the pure-tone audiograms were assigned to one of three categories: (1) no bone response, hence no air-bone gap (Fig. 1); (2) bone responses up to and including 1000 cps with an air-bone gap (Fig. 2); and (3) bone responses at only 250 and 500 cps with an air-bone gap (Fig. 3). Categories 1 and 3 are generally diagnosed as sensorineural loss, category 2 as mixed (sensorineural and conductive) loss.

There was a high incidence of audiograms (74%) in category 3. A lesser number (21%) fitted into category 1 and 5% fitted into category 2. The incidence of bone responses at only 250 and 500 cps was greater, the incidence of no bone conduction responses approximately the same, and the incidence of bone responses up to and including 1000 cps was less than reported by McConnell & Bowman (1963) for a group of hearing-impaired young adults. Such a comparison indicates that the children in the present

Nober (1964) has pointed out that if bone responses are tactile at some intensity levels oscillators bone should not be calibrated beyond certain limits

The objectives of the present study were to gather information from a group of severely hearing impaired children relevant to the following questions

(1) What is the incidence of a pronounced low frequency air bone gap?

(2) What is the incidence of an absent vestibular response?

(3) What is the relationship between hearing sensitivity as determined by conventional audiometry and vestibular responsiveness as determined by electronystagmography?

METHOD

Equipment

Audiometry

A Maico MA-8A audiometer in an IAC soundproof room was used for all pure tone testing The acoustic output of the audiometer was calibrated at two week intervals to meet the 1964 ISO requirements.

Electronystagmography

Silver disc electrodes connected to a Grass Model 5 Polygraph were used to record eye movements in the horizontal and vertical planes The time constant of the two channels used to record these movements was 3 seconds The water for the hot and cold irrigations was kept at 44 C and 30 C respectively in Haake model S thermostatically controlled circulating pumps The thermostats were adjusted to give the quoted temperatures at the irrigating nozzle

Subjects

In all 25 children (13 boys, 12 girls) enrolled in the Montreal Oral School for the Deaf were tested They ranged in age from 7 to 15 years with a mean age of 10 5 years The loss in six children was associated with maternal rubella in two with rhesus incompatibility one with maternal goiter one with meningitis, and one with maternal flu In three children the loss appeared familial and the etiology was unknown in the remaining 11 cases

Procedure

Audiometry

Each child was tested by conventional audiometry (air and bone conduction) at 10 frequencies (125 250 500 1000 1500 2000 3000 4000 6000 and 8000 Hz) The right ear was tested first in half of the children the left ear first in the other half Because the thresholds of the two ears for a given frequency never differed by more than 35 dB masking was never required to prevent participation of the non-test ear

Electronystagmography

The procedure used is essentially that described by Fitzgerald & Hallpike (1942) except that eye movements are recorded electrically and the eyes were kept closed during caloric testing. The silver disc electrodes were positioned one immediately lateral to each eye to record the horizontal nystagmus, and one above and below the left eye to record the vertical nystagmus. A ground electrode was positioned in the centre of the forehead.

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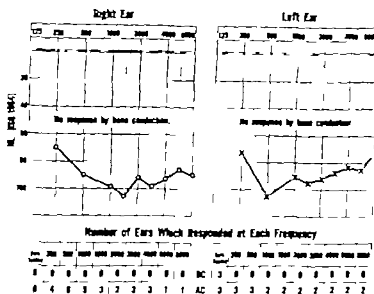


FIG. 1 Mean right and left ea air and bone conduction thresholds for the hildren with sensorineural type losses.

study responded to fewer frequencies by bone conduction than the young adults in McConnell and Bowman s study

The Incidence of an Absent Vestibular Response

The results of electronystagmographic testing were grouped into two categories of response present and absent In 10% of the ears there was no response in the majority (90%) a response was present The incidence of response was greater and the absence of response less than reported by

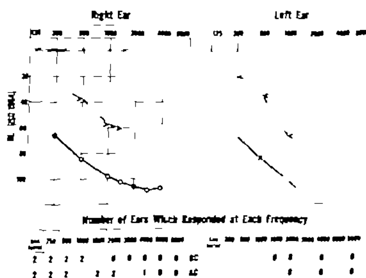


FIG. 2 M n right and l ft ear l nd bo conduction threshold fo the children with mixed-type (s sorineural d cond cti n) losses.

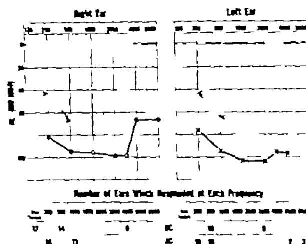


FIG. 3. Mea right nd left ea ai and bone conduction thresholds for the children with pronounced low frequency l -bone gap.

McConnell & Bowman (1963) A Chi square analysis of the data dem n trated that the differences in results between the present study and th t of McConnell and Bowman in category of vestibular response was significant (< .01) The lower incidence of absent responses in the present sample may reflect th greater sensitivity of electronystagmographic re cording as compared with direct observation of the nystagmic responses, differences in strictnes of criteria on the part of the tester or differences in samples.

The Relationship Between Auditory and Vestibular Responses

One of the problems in relating auditory and vestibular responses is the deci ion as to which measure of auditory sen itivity to use bone conduc ti m ai conduction. In con idering this we have related the presence or absence f estibular response to both bone and air thresholds.

F r the first comparison the audiograms were di ided into two groups b ne response present or bone response absent Table 1 presents the two groups of bon conduction responses a a function of the two groups of estibul r responses. The Fisher exact test nalysis (Seigel, 1956) of these data indicated a significant association (< .02) between bone and estibular responses.

Bocca & Perani's (1960) theory is supported by those results in Table 1 76 and 4) which indicate that the presence or absence of a bone conduction response coincided with the presence or absence respectively of a vestibular response The remaining two categories show that their ex planation does n t pply in all cases no vestibular response with bone conduction response (6%) and vestibular response with no bone conduc

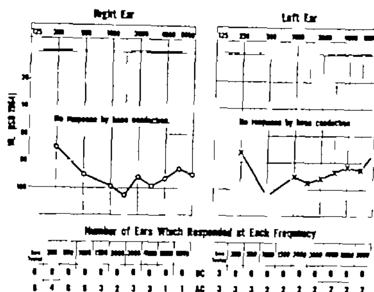


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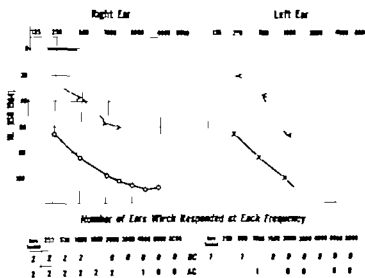


Fig. 2 Mean ight and l ft air d bo conducti n thre hold for the hildren with m xed-type (nsorineural and c duction) losses.

used Three groups were then formed based on the average response at the speech frequencies <90 dB, 91–97 dB and >98 dB The results of this grouping are presented in Table 2 which shows that all of the ears with no vestibular response had an average loss by air conduction greater than 98.0 dB (107 7 111 7 113.3 115 and 115 dB) Thus, there appears to be a strong tendency for absent vestibular responses to be associated with very poor air conduction thresholds. This finding is in accordance with the results reported by Sandberg & Terkildsen (1965)

In general it appears that vestibular responsiveness gives some information about both measures of auditory sensitivity The presence of a vestibular response suggests that bone conduction responses are present but gives little information concerning air conduction thresholds. The absence of a vestibular response gives little information concerning bone conduction responses, but suggests that the hearing loss by air conduction is very severe

As other investigators have found (Rosenblüt *et al.*, 1960 Sandberg & Terkildsen 1965) the present results indicate that the general relationship between auditory and vestibular responses is of negligible value in determining the degree of hearing loss in individual cases. They also preclude the adoption of a single theory to explain the occurrence of a low frequency air-bone gap

ZUSAMMENFASSUNG

An iner Gruppe von 25 Ki dern mit schweren Hörschädigungen wurden die Hörschwelle für Luft und Knoche l itung ufgenommen und mit den Befunden des kalorischen Tests der Vestibularf nktion, die durch Nystagmusregistri rung festgest llet wurde erglichen Wie die Untersuchungen ergaben entspricht in der weitaus überwi genden Zahl der Fäll einer positiven Vestibularreaktion eine messbare Knochenleitungshörschwelle während zwischen positiver Vestibularreaktion un l der Höhe des Luftleit ngshörverlustes keine besondere *Zuord nung* zu erken en ist andererseits ist der Ausfall der Vestibularreaktion *mit einem* schweren Luftleitungshörverlust verbunden während die *Knochenleitung* in diesen F llen t l messbar und t ils nicht messbar ist. Aus der *K ntakts* der Vestibularreaktion llein lässt sich also im individuellen Falle ni hts genaueres uber da *betreffende Hörvermögen aussagen Di l der grossen Mehrzahl der* Fäll zu verz ichnend Luftleitu gs-Knochenleitungs-Diastase im tiefen Frequenzberei h la st sich weder durch di Annahme ines *vestibulären Hörmechanismus* noch durch Deutung der Knochenleitungsreaktion ls rein taktil in allen Fällen h nreichend erklären

RÉSUMÉ

Les seuils osseux et aé iens d'un groupe d 25 enfants yant u surdité profonde nt été mesurés et comparés aux résultat des test caloriques pour la fonct on vestibulaire enregistrés par l'électronystagmographi Quoique la p é sence d'un réponse vestibulaire soit généralement reliée à la présence de réponses osseuses mesurables, mai non à des seuil aériens, et que l'absence d une réponse estibulaire soit reliée à un perte aérienne sé ère mai on ux seuils

TABLE 1 *Number of ears classified by auditory (bone conduction) and vestibular responses*

	Bone conduction response	
	Present	Absent
Vestibular response		
Present	38 (6 %)	7 (14)
Absent	3 (6 %)	2 (4)

tion response (14%) The former show that bone responses can occur in the absence of vestibular responses The latter suggests that vestibular responsiveness is not always asociated with low frequency bone hearing, although in this instance the possibility exists that hypoactivity of the vestibular mechanism raised the bone threshold beyond the limits of the audiometer

The results (76% and 6%) in Table 1 which indicate that a bone conduction response was present are in accordance with Nober s (1964) theory of "tactile hearing There are however ears (14% and 4%) from which no bone response was elicited a finding which suggests that tactile exteroception does not always result in pseudo-bone-conduction responses. In three children there was no response to bone conduction unilaterally with low frequency bone responses in the other ear This finding would not be in accordance with Nober s theory unless 'tactile hearing" can occur unilaterally

For the second comparison the air conduction data were categorized in the manner used by Sandberg & Terkildsen (1965) That is, the threshold for each child at the three speech frequencies (500 1000 and 2000 cps) were averaged When there was no response at a given frequency a value of 5 dB above the maximum output of the audiometer for that frequency was

TABLE 2 *Number of ears classified by auditory (air conduction) and vestibular responses*

	Vestib lar response		
	Prese t	Absent	T tal
Average air condu tion response I dB (re iso 1964)			
≤ 90 (range 76,7–88.3)	6	0	6
91–97 (rang 91.3–96.7)	8	0	8
≥ 98 (range 98.3–115)	31	5	36
T tal	45	5	50

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FURTHER INVESTIGATIONS ON CORTICAL DEAFNESS

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An investigation of functional alterations following temporal lobectomy for focal epilepsy leads to some considerations of auditory physiopathology. In some cases Heschl gyri were sacrificed in the surgical removal, in other cases they were spared. A speech discrimination impairment of the same degree was found in both cases.

It is well known that sensitized speech audiometry has made an important contribution to the assessment of cortical auditory disorders as a sufficiently well defined clinical form.

This type of dysacusis has been investigated by a large number of authors who agree that sensitized speech-tests produce asymmetric discrimination figures in patients with lesions of the temporal auditory cortex (Bocca *et al.* 1954, Goldstein *et al.* 1956, Bocca *et al.* 1957, Greiner & Lafon, 1957, Matzker 1957, Bocca 1960, de Quiros, 1960, Jerger 1960, Bocca & Calearo, 1963, Jerger 1964, Kirikae *et al.* 1966, Hodgson, 1966). Unquestionably on account of the absence or poor significance of pure-tone threshold changes, this defect of auditory integration, which is nearly always contralateral to the site of the cortical lesion and appears to be independent from hemisphere dominance (Calearo & Antonelli, 1963), seems to be highly indicative.

Up to now this type of dysacusis has always been related to damage of the primary cortical auditory area at the level of Heschl's gyri.

In this field recent experience has pointed to some new aspects of the problem, which we are now going to present. Our observations concern the influence on the integration processes of the auditory message exerted in man by removal of the cortex.

It is indisputable that this process is of great significance for definition of the function of the cortical auditory area. As compared to data established on post-mortem (mostly tumoral) pathology of the acoustic temporal cortex, where it is often difficult to define the extension of the lesion, the study of auditory function following temporal lobectomy undoubtedly offers the advantage of correlating the qualitative and quantitative aspects of the post-operative hearing function with the anatomical limits of surgical removal.

Eleven adult male subjects (aged between 41–58) suffering from repeated attacks of temporal lobe epilepsy resistant to usual medical treat-

osseux — la relation entre les réponses auditive et vestibulaire est le valeur négligeable dans des cas individuels, pour prédire les seuils auditifs d après les réponses vestibulaires. Ni la théorie de l audition vestibulaire ni celle de l'audition tactile seules, ne peuvent expliquer tous les audiogrammes présentant une courbe sévère à composante conductive apparente

ACKNOWLEDGMENTS

Miss Rosemary Schilling electronystagmography technician is thanked for her invaluable assistance

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cortical auditory area enclosing the primary one the existence of a secondary cortical area has not been demonstrated in man, but animal experiments have shown cortical organisation for the mechanisms of hearing reactions to be much more complex than expected

These theories are not necessarily in conflict The former two are supported by evidence of functional defects in the contralateral ear before surgery in some cases where macroscopic observation of the cerebral tissue at the level of the primary auditory area failed to show any sign of anatomical lesion of the sites where electroencephalography and electrocorticography had diagnosed an epileptic focus It is further of interest that in nearly ll cases extensive lobectomy for larger lesions led to more marked defects of auditory integration

Even the hypothesi of the presence of a secondary auditory area appears to be most interesting and we consider it significant to be able to state it for the first time in the light of these clinical data which—in any case—throw further light on the functions of the auditory cortex and on the mechani ms of thi complex nervous function

Finally these data throw further light on the possible existence of a secondary cortical auditory area where complex integrative mechanisms take place

ZUSAMMENFASSUNG

Die funktionell n Störungen nach Schläf nlobektomi für Epilepsi gestatten e n g Betrachtungen über die Hörphysiologie und Pathologie Der wi htigste Befund war d ständige Bew l ines Sprachdiskriminatio sverlustes un bhän gig von der Ausbreit g der hirurgischen Beseitigung im Schläfe lappen el e Diskrimination störung wurd bemerkt, auch w nn da primäre Hörri denfeld geschont wurde

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FIG 1 Brain section at a di tance of 38 mm from the median agittal pla 1 Plane f classical lobect my 2 plane of lobectomy comprising posterio ly Heschl's gyri

ment were admitted to the Neurosurgical Clinic of the Milan University for surgical removal of the affected temporal lobe After extensive neurological examination the sensitized speech tests which are already well known and have been recently summarized (Calearo & Antonelli 1967) were performed before surgery In all cases the temporal lobe involved and surgically removed was the right one so that problems connected with sensory aphasia were out of the question

We should like to stress here the most interesting finding, i e that auditory integration has been found to be reduced after the operation This finding was present in all cases, whether or not the surgeon had removed Heschl s gyri, considered to be the site of the primary auditory area (Fig 1)

This finding which has been confirmed later (Jerger 1964) appears to be of the greatest interest for the solution of the complex problem of cortical acoustic physiopathology

Its interpretation is not an easy one actually the lack of concordance between the anatomical and the functional lesions might be explained —in the light of the data available up to now—by a number of different theories viz. (1) the cortical auditory area in patients suffering from temporal lobe epilepsy is affected preoperatively by a lesion which alters its function the hearing defect remains unmodified regardless of partial removal of the temporal lobe (2) surgery (or the spontaneous lesion itself) leads in due course of time, to local pathological (oedema haemorrhage etc) or functional (irritation of nerve fibres, von Monakow s diaskysis etc) changes which are capable of alterating the function of cortical or subcortical areas close to the lesion or having neuronic relationships with it This view indicates that whenever Heschl s gyri are left intact and the speech discrimination defect is due to this temporary decrease of function the postoperative defect is bound to regress as soon as local irritative conditions caused by the intervention gradually disappear Conversely whenever Heschl s gyri have been removed this possibility is lacking thus, if we believe them to be solely responsible for a satisfactory hearing integration we might only consider the possibility of compensation by the contralateral hemisphere (3) temporal lobectomy affects an hypothetical secondary

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A SECRETORY AND CLINICAL INVESTIGATION OF THE PAROTID GLANDS IN PATIENTS WITH RHEUMATOID ARTHRITIS

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An investigation was carried out to ascertain whether the salivary secretion of the parotid gland is lower in individuals with rheumatoid arthritis (RA) than in healthy individuals—control group (C) and whether parotid involvements and oral symptoms are more common in an RA group than in a C-group. The investigation was performed on 92 patients with rheumatoid arthritis and 92 control patients of corresponding sex and age. Salivary secretion was recorded during rest, stimulation with 1 and 6 per cent citric acid and stimulation with intravenously administered acetyl-beta-methylcholine iodide Betacholyl® (MeCh) with a dose of 0.2 mg/min.

The investigation produced the following results: (1) The rate of parotid secretion is significantly lower in the RA-group than in the C-group on stimulation with 1 and 6 per cent citric acid and almost significantly or significantly (log value) lower on stimulation with Betacholyl with the dose of 0.2 mg/min. (2) Individuals with subjective xerostomia are almost significantly more common in the RA-group than in the C-group. (3) The RA-group has significantly fewer intact teeth and a significantly greater number of edentulous subjects or subject with full dentures. (4) The correlation coefficients between resting secretion, citric acid stimulated secretion and Betacholyl stimulated secretion within the C-group are very low. An analysis of the correlation coefficient shows that there are grounds for assuming that the factors or the significance of the factors affecting secretion vary with the type of stimulation.

The possibility of a connection between rheumatoid arthritis and impaired function of the salivary glands was first suggested by Sjögren who in 1933, described from an ophthalmological point of view a syndrome characterized by keratoconjunctivitis sicca (KCS) and rheumatoid arthritis (RA) or xerostomia or both of these signs. While considerable attention has been devoted to the connection between KCS and RA since Sjögren's pioneering work (Holm 1949, Henderson 1950, Thompson & Eadie 1956, Blatz, 1961) the relation of xerostomia or hyposalivation to rheumatoid arthritis has not been made the object of any systematic analysis.

Accounts of investigations of the functioning of the salivary glands in cases of rheumatoid arthritis have earlier been given only by Günther (1950) and Brémová *et al* (1962) In an examination of 30 rheumatoid arthritis patients (with no further description of the patients or the methods used) Günther found a generally lower volume of saliva in these than in 20 healthy individuals Brémová *et al* determined the total saliva in 250 patients with rheumatoid arthritis during 15 minutes rest and 15 minutes while chewing paraffin Xerostomia was considered to exist in 14 per cent of the cases, those with a secretion volume of less than 9.5 ml This value was obtained by halving the mean value (19 ± 14 ml/hour) arrived at by Becks & Wainwright (1943) in an examination of healthy volunteers

The purpose of our investigation is to provide answers to the following questions

1 Are there quantitative differences in the salivary secretion of the parotid gland between individuals with RA and those in a control group?
2 Are differences if they exist independent of the form of stimulation applied?
3 Are parotid involvements and symptoms of xerostomia more common in individuals with RA than in those who are healthy in this respect, and are there differences in the oral status between the groups

MATERIAL

The material is comprised of 184 individuals, 92 with RA and 92 healthy in this respect (C)

The Rheumatoid Arthritis Group

The material consists of in patients at the Rheumatological Subdivision of the Department of Internal Medicine at the Umeå Hospital All the in patients who at the time for the investigation and according to the criteria of the ARA (American Rheumatism Association Hollander 1960) have been diagnosed as cases of rheumatoid arthritis (classical definite or probable) have been requested to take part Of altogether 103 patients it has been possible to use 94 The age among the 61 women varies between 26 and 64 years with an average age of 49.5 years among the 31 men between 26 and 64 years, with an average age of 48 8 years An account of the RA groupe is given in *Table 1*

All the cases have been considered to be in the clinically active phase of rheumatoid arthritis, judged on the basis of joint swelling, morning stiffness tenderness and pain in connection with movement However three men and eight women have no surely raised sedimentation reaction (ESR < 20 mm/hour)

T[illegible] 1. *D[illegible]gnostic data in 93 patient[illegible] with rheumatoid [illegible]rthritis.*

Diagnosis (ARA)	Sex M	Sex F	Duration of the disease (years) Mean M	Mean F	Mean M F	Range	Rheumatoid progression stage (Steinbrocker *et al.*, 1949) I II M	I II F	III M	III F	IV M	IV F	Positive titers SSCAT 1/80 M	SSCAT 1/80 F	ALT 1/10 M	ALT 1/10 F	ESR mm/1 hour Mean M	Mean F	M F	Range
Classical	19	39	10.8	12.4	11.9	1–38	4	4	11	16	1	19	15	35	18	38	46.8	51.3	49.8	10–96
Definite	12	19	4.1	9.1	7.2	0.5–21	11	10	1	4	0	5	8	4	10	0	31.8	31.9	31.8	2–58
Probable	—	3	—	0.8	0.8	0.5–1	—	3	—	0	—	0	—	0	—	0	—	25.3	25.3	8–17

Sex	Positive titers AST 200	ASTA 2.5	Hb g/100 ml Mean	Range	Eosinophilic leucocytes 4	Total serum protein and paper electrophoretic fractions g/100 ml: Albumin Mean	Range	Alpha₁-globulin Mean	Range	Alpha₂-globulin Mean	Range	Beta-globulin Mean	Range	Gamma-globulin Mean	Range	Total protein M	Range
M	4	7	12.6	0.5–11.6	1	1.8	2.8–6.1	0.2	0.1–0.4	0.1	0.2–0.7	0.6	0.2–0.9	1.1	0.7–3.1	7.5	6.5–8.1
F	10	13	11.7	8.7–13.9	13	1.7	3.2–6.2	0.3	0.1–0.4	0.4	0.1–0.8	0.5	0.2–0.9	1.6	0.6–5.9	7.5	6.0–10.2
Total	14	20	12.0	8.7–11.6	17	1.8	2.8–6.1	0.2	0.1–0.4	0.4	0.1–0.8	0.6	0.2–0.9	1.5	0.7–5.9	7.5	6.0–10.2

T[illegible] 2. *Diagnostic dat[illegible] [illegible] 93 pat[illegible]nts in the control series*

Sex	ESR (Westergren) Mean	Range	Eosinophilic leucocytes 4	Hb* g/100 ml Mean	Range	Positive titers SSCAT >1/80	ALT 1/10	Positive titers AST >200	ASTA >2.5	Total serum protein and paper electrophoretic fractions g/100 ml: Albumin Mean	Range	Alpha₁-globulin Mean	Range	Alpha₂-globulin Mean	Range	Beta-globulin Mean	Range	Gamma-globulin Mean	Range	Total protein Mean	Range
M	10	2–36	3	11.3	11.7–17.2	1	1	9	3	5.6	1.0–6.7	0.1	0.1–0.3	0.2	0.1–0.4	0.4	0.2–0.6	0.8	0.3–1.2	7.1	6.8–8.3
F	12	2–33	1	13.0	9.0–16.1	0	1	12	5	5.6	1.0–6.5	0.1	0.1–0.3	0.2	0.1–0.3	0.4	0.1–0.7	0.8	0.1–1.5	7.2	5.1–8.3
Total	11	2–36	7	13.5	9.0–17.2	1	2	21	8	5.6	1.0–6.7	0.1	0.1–0.3	0.2	0.1–0.1	0.4	0.1–0.7	0.8	0.3–1.5	7.2	5.1–8.3

15.8 100%. M 3 cases > 20; F 8 cases [illegible] 20. [illegible] 01

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Sialometric method

The method applied for the determination of secretory rate is a modifica tion of a method described by Diamant *et al* (1957) which has been de veloped and described in detail by Enfors (1962)

The secretory determinations have been made during rest and during timulation The stimuli have consisted of intravenously administered acetyl betamethylcholine iodide, MeCh (Betacholyl® Vitrum Stockholm) and intra orally administered citric acid solution in two concentrations.

A compared with the method described by Enfors, modifications have been made with respect to

1 Instillation of the 6 per cent citric acid
2 Drop computer
3. Course of examination.

After a preliminary rinsing of the mouth cavity with water and a resting period of about 5 minutes, the secretory determinations were carried out in accordance with the following routine

1 Secretion during relative rest
2. Betacholyl stimulated secretion 0.2 mg/min continuous administra tion
3. Citric acid stimulated secretion, 1 per cent solution at the dorsum of the tongue 3 drops every 30 seconds.
4 Betach lyl stimulated secretion 0.3 mg/min continuous administra tion
5 Citric acid stimulated secretion, 6 per cent solution at the dorsum f the tongue 3 drops every 15 seconds.

Recordings were made during 5-minute periods except for the 6 per cent citric acid solution, for which the time was 2 minutes. Between recordings, the mouth was carefully rinsed with water and th tubes flushed out The interval between the stages varied, depending upon how quickly the glands returned t resting secretion A fresh stimulus was administered at the earliest 5 minutes after this.

Secretory determination for all materials were made with the same m thod and apparatus and at the same hours of the morning and after noon.

SECRETORY METHOD ANALYSIS

E rors due t th apparatus

Th tability of the infu ion apparatus was checked at the two rates used f the experimental series by weighing the liquid pumped out in the course of minutes. Usi g an 0 02 per cent Betacholyl solution the dose would be an a erage of 0.204 nd 0.311 mg/min respectively f r the two rates of administration (N = 6 f r each rate)

None of the patients was at the time of the examination completely confined to bed or febrile Apart from a patient with insulin treated diabetes, no diseases besides rheumatoid arthritis have been diagnosed which have in the light of earlier experiences proved able to result in parotid involvement

The Control Group

As earlier investigations have indicated that the factors of age and sex may influence the rate of secretion of the salivary glands (Meyer & Necheles, 1940 Lourie 1943 Nash & Morrison 1949 Kullander & Sonesson 1965) the control material has been selected from the clientele of the School of Dentistry in Umeå according to the following principles

Taking the age and sex distribution of the RA series as point of departure a "twin has been taken as random sample by selecting from the registration list at the School of Dentistry s out patient reception beginning from the 1 1 1965 the first individual domiciled in Umeå who in sex and age has within ±2 years had a counterpart in the RA series, which was at the outset set up in alphabetical order If the random selected control patient has had a diagnosed rheumatoid arthritis, he (or she) has been excluded and replaced by the next in order who met the requirements mentioned Of altogether 97 individuals summoned 93 came for examination while 4 failed to put in an appearance One case was excluded during the investigation An account of the C group as to laboratory data is given in Table 2

METHOD

The following examinations have been performed routinely

History with the main stress on sicca symptoms and signs and current or former pathological states in the facial cervical or auricular regions.

Physical examination with recording of extraoral and intraoral findings such as changes in the mucous membrane, rhagades at the corner of the mouth swellings and palpation findings over the parotid region The dental status has been taken by recording the number of intact teeth and noting whether or not the patient wore full dentures

Laboratory examination of the secretory volume of the left and right parotid glands

The examinations have been identical for the RA and C groups and have been carried out by one and the same investigator

Numerical and statistical analyses have been performed for the most part with a data processing computer Generally accepted methods were used for the calculation of the mean values, standard deviations and errors, and correlation coefficients Student s *t*-test was used to determine the level of significance $0.05 > P > 0.01$ $0.01 > P > 0.001$ $P < 0.001$

TABLE 3 *The mean values ($\bar{x}$) and the errors of the mean ($\varepsilon_{\bar{x}}$) in the RA and control-series (C) for the secretion values*

N 82 for resting and citric acid stimulated secretion and for Betacbol 1 stimulated secretion 82 (RA) and 85 (C) respectively The levels of significance are marked ith asterisks.

Variabl	RA	C	Difference RA − C	Level f signifi-cance
	$\bar{x} \pm \varepsilon_{\bar{x}}$	$\bar{x} \pm \varepsilon_{\bar{x}}$	$\bar{x}_{RA} - \bar{x} \pm \varepsilon$	
Resting secretion L/5 min	3 77 ± 0.83	3.07 ± 0 82	0. 0 ± 0.72	
Resting secretion R/5 min	4.21 ± 0 69	3 53 ± 0.34	0 71 ± 0 7	
Resting secretion L R/5 min	8 01 ± 1.30	6.60 ± 0.63	1 41 ± 1.44	
1 citric acid L/5 min	32 80 ± 2.41	50 99 ± 3.46	−18 19 ± 4.23	
1 citric acid R/5 min	33.16 ± 2.30	53 98 ± 3.70	20.82 ± 4.35	**
1 citric acid L + R/5 min	65.97 ± 4.51	104.97 ± 6.93	−39.00 ± 8.26	***
6* citric acid L/3 min	43.11 ± 2.90	59 46 ± 2.77	−16.35 ± 4 01	
6* citric acid R/2 min	42 23 ± 2.85	59.92 ± 2.86	−17.67 ± 4.04	
6* citric acid L R/3 min	85 37 ± 5 51	110.38 ± 6.36	−31.02 ± 89	
Betacholyl 0.2 mg/min L/5 min	49.32 ± 3.96	60 32 ± 4.00	−11.00 ± 5.64	
Betacholyl 0.2 mg/min R/5 min	49 62 ± 4.24	61.51 ± 4 20	−11.89 ± 5.97	
Betacholyl 0.2 mg/min L R/5 min	98 82 ± 8.11	121.83 ± 8 12	−22.97 ± 11.47	
1 citric acid L R/5 min. Log alue	3.93 ± 0.096	4.55 ± 0.054	− 0.58 ± 0.10	
6* citric acid L R/2 min. Log value	4 22 ± 0 061	4 70 ± 0 042	− 0.18 ± 0.094	**
Betachol 1 0.2 mg/min L R/5 min. Log value	4 14 ± 0 129	4.55 ± 0.063	− 0 41 ± 0 153	**
Betacholyl 0 3 mg/min L/5 min	(*)	98.61 ± 5.25		
Betacholyl 0 3 mg/min. R/5 min	(*)	101.33 ± 5 68		
Betacholyl 0 3 mg/min. L + R/5 min	(*)	199.94 ± 10.60		
Betacholyl 0 3 mg/min. L R/5 min. Log alue	(*)	5.16 ± 0.062		

Not investigated.

if there i no difference By matching pairs, the possibility increases to urely evaluat the differences in secretory flow between the groups. The result in Tables 3 and 4 agree.

The resting secretion shows no differences in Tables 3 and 4 between the RA and C-groups. The number of glands with non-recordable values for resting secretion (zero alues) is, however twice as great (39) in the RA group as in the C-group (19) The difference is significant (<0.01) The v lume of secretion for the C-group agrees with the result earlier arrived at by Enf rs (1962)

The connection between the secretory responses on the right nd left ides for different stimuli was investigated for the C-group For all stimuli there i high and trongly ignificant correlation between the parotid gland of the right and left ides. The highest correlation i for the Betacholyl stimulated secretion (resting secretion $r = 0.81$ stimulated secretion with citric acid 1% solution $r = 0.80$ 6% $r = 0$ 9 and with MeCh 0.2 mg/min $r = 0$ 07 0.3 mg/min $r = 0.0_3$)

The counting systems for the right and left sides were investigated for three rates (low mediate high N = 6 for each rate) The mean values for the size of drop in the three experimental series were calculated They were 0 061 for the right system and 0 059 g for the left system The difference between the right and left sides is not statistically significant.

Errors due to the individual

*In order to study the systematic error and variability within the in*dividual comparisons were carried out for a number of healthy individuals (N = 11) between the secretion on a first (*IN*1) and a second (*IN*2) experimental occasion For every stimulus, the determinations were carried out with an interval of seven days and in exactly the same way The double *determinations* have been analysed with reference to the correlation coefficient between the *IN*1 and *IN*2 values, the mean value and the standard deviation for *IN*1 minus *IN*2, as well as the mean value and the standard error of the mean value for the quotient $|IN1 - IN2|/IN1 \times 100$

The quotient has been formed as an absolute number and according to definition been provided with a positive sign It may be seen as an expression for the relative magnitude of the total systematic error and includes inter and intra individual biological variations, variation due to the experimental apparatus and possible systematic changes in the amount of secretion between *IN*1 and *IN*2

The following conclusions can be drawn from the analysis of the method

1 The systematic errors due to the infusion and recording apparatus are slight compared with the variation found among the subjects

2 The biological variation between the individuals is greater than the *intra individual variation and the systematic error due to the apparatus.* The method thus has sufficient accuracy for comparisons between groups of individuals

3 The citric acid stimulated secretion shows less intra individual variation than the Betacholyl stimulated secretion

RESULTS

Secretory

Table 3 shows the mean value ($\bar{x}$) and the standard error of the mean value (S E.) for the salivary secretion with different stimuli in the RA and C groups, and the mean difference between the mean values and their standard errors It also shows conversions of the original values through calculation of the natural logarithms

Table 4 gives the formation of quotients between the RA and C groups obtained within matching pairs for non-stimulated secretion and stimulated secretion (citric acid 1% 6% and MeCh 0.2 mg/min) Such quotients may vary theoretically *from* −1 to +1 and they should on an average be 0

The effects of rheumatoid arthritis on parotid secretion have not been elucidated but roentgenological (Ericson, 1967) and clinical investigations of similar material indicate parotid destruction Other causes of differences in secretion may conceivably be differences in the general state of health and the use of prescribed medicines. The connection between rheumatoid arthritis and reduced salivary secretion will be analysed in a separate work (Ericson 1968)

The importance of saliva for the dental status is well attested The RA group had a higher caries rate a lower frequency of intact teeth and a higher frequency of full dentures This may be related to the differences in secretion However other factors, such as diet illness, as well as a changed dental-care situation due to illness also affect the dental status.

ZUSAMMENFASSUNG

Bei 92 Patienten mit rheum tischer Arthritis und 92 gesu d Verglei hspersonen wurd die Speich lsekretion vor sowie ach Stimulierung mit 1 und 6%iger Zitro ensäure u d mit In ei er Dosi von 0,2 mg/ml L zug führten Betach lyl? gemessen Zweck der Untersu hung w feststellen ob die Sekretion der Glandula P roti bei Patienten mit rheumatischer Arthritis geringer ist nd gl ichseitige Veranderungen in der P rotis und rale Sympt me bei Arthritis-Kra ken hä figer sin l als bei Gesu d

Die Ergeb isse la sen ich wi f lgt zusammenfassen 1 In der Arthritis-Gruppe ist die l rot ssekret bei Stim lierung mit 1 und 6%iger Zitronensäure sta t stisc] *gn l kant nd bei Stimulieru g mit Beta hol l naheru signifikant oder* ignif kant grösser l in der Ko trollgruppe 2. Subjektive Xerostomie kommt der Arthr tis-Gruppe haufiger vor der U terschied ist statistisch naheru ig-if ka t. 3 Die Anzahl gesunder Zah ist l der Arthritis-Gruppe ignifikant geringer un l ll Anzahl zahnloser oder ollprothesetragender l ersonen st tistisch signif k nt grösser 4 Der Korrelationskoeffizient zwischen Ruhesekretion und Sekretion nach Zitronens] re un l Betacholyl ist l der Gruppe der Gesunden seh nied g. Ein n here A lyse ler Korrelationsfakt ren legt den Schl s nah da die di Sekretion beei flu senden Faktoren bzw ihre Bedeutung mit der Art der St mulierung rlieren

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secretion are strongly significant and for Betacholyl stimulated secretion almost significant or significant (L+R) This seems to indicate that there is a clear-cut connection between reduced parotid secretion and rheumatoid arthritis The investigation agrees in this respect with the works referred to in the introduction (Günther 1956 Brémová *et al.*, 1962) However because of the inherent nature of clinical investigations the possibility cannot be excluded that there were facors other than rheumatoid arthritis which may have had an effect on salivation (Differences due to age and sex were taken into consideration)

It is noteworthy that the Betacholyl stimulated secretion shows less significant differences between the RA and C-groups than does the citric acid stimulated secretion The explanation of the discrepancy probably lies chiefly in the decisive differences between the mode of stimulation

Betacholyl for example, acts directly upon the gland as a parasym pathomimetic while the citric acid acts via receptors and reflexes. According to Schneyer & Hall (1965) stimulation with pilocarpine and acetyl betamethylcholine iodide cannot be substituted for reflex stimulation as reflex stimulation by feeding probably evokes activity in sympathetic as well as parasympathetic fibres Other probable explanations of the relative differences between citric acid and Betacholyl stimulation are the greater differences in the individuals as regards of the Betacholyl stimulation As the RA group showed on an average a significantly lower body weight (~ 7 kg) than the C group and as the Betacholyl dosage was given in a standard dose the RA group may on the average have been stimulated more than the C group Also of importance is the fact that ten subjects in the RA group did not participate in the Betacholyl experiment, chiefly because of medical reasons Most of the ten were severe RA-cases who showed values lower than the mean value for citric acid stimulation

There are weak or even negative connections between resting secretion, citric acid stimulated secretion and Betacholyl stimulated secretion It is, thus, suspected that there are different factors of importance of salivary secretion operating in these three forms of parotid secretion The result of the application of the tetrad criterion to the correlation coefficients col laborates this view This must be taken into consideration when the results from investigations with different parotid stimuli are compared *The results from one form of stimulation do not necessarily apply to results from another*

A comparison between the correlation coefficients for the right and left sides within the same individual for resting secretion and citric acid stimulated secretion shows that the coefficients are of the same order of magnitude $r \sim 0.80$ For the Betacholyl stimulated secretion r is not less than 0 95 The higher value for the Betacholyl is probably due to the intravenous mode of stimulation From the high correlation coefficients for Betacholyl it may be deduced that the salivary secretions of the right and left parotid glands are usually very close to each other

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CONSTRUCTING A NEW BONY POSTERIOR CANAL WALL IN ELIMINATION OF THE RADICAL MASTOID CAVITY

Use of Pedicled Temporal Bone-periosteum Flap

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An operation is described which was devised to reconstruct a new bony posterior canal wall using temporal bone-periosteum pedicle flap. We feel that this is not only advantageous in the obliteration of the mastoid cavity but will also enhance subsequent functional surgery. This method was utilized in four patients with effective results. The first two patients did not have mastoid-cavities to start with. Their posterior canal walls were taken down unsparingly at time of operation for chronic disease of the tympanic cleft and one-stage reconstruction performed. It is suggested that this addition to the technique of Rambo might significantly rehabilitate our "aural cripples" as indicated by our present experience.

With recent advances in microsurgery of the ear it would appear that fewer mastoid cavities are iatrogenically created. The patient with the "mastoid cavity" is an aural cripple requiring regular toilet. He is limited in aquatic sport by the effects of wetting the cavity and the exposure of the horizontal semi-circular canal.

The work of Mill (1930) and Rambo (1952) paved the way for this new concept of mastoid obliterative surgery, stimulating contributions in this field by Schiller (1963), Pal a (1963) and Sadé (1963). With these as a basis, the present operative approach to constructing a new bony posterior canal wall was devised. On close review of the literature the authors have been unable to find a similar procedure described in the literature.

METHOD

A post-auricular incision is made in the hairline through skin and subcutaneous fascia from the temporal region to just below the mastoid tip. This skin flap is elevated posteriorly and anteriorly as far as the conchal cartilage. An incision is then made just posterior and parallel to the conchal cartilage through the remaining soft tissue down to, but not through, the

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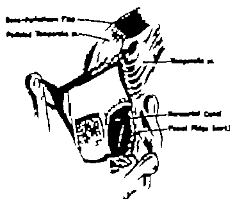
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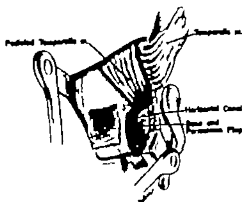
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FIG. 3. Flap mobilized prior t ad ancement.
FIG. 4 Pedicl 1 position "new bony posterior canal w ll"

Case Reports

1 S. C., a 30-year-old female who ince the age of 10 ha had a "chronic running right ear In 1962 a mastoidectomy was performed which was revised in 1964 At thi time ch lesteatoma was reported The mean hearing loss f r air and bone conduction was 50 and 8 dB respectively In 1965 it was reported that there was recurrent cholesteatoma and that a good por tion f the posteri r can l wall wa defective with a large marginal-attic perfo ation Eustachian tube patency was described. A further mastoidec t my-tympan plasty was carried ut. Choleste tomatous tissue was present in the niche of the round and oval windows. On examination in March 1966 a persistent "running ear" wa found The major portion of the tympanic membrane was deficient while an nnular rim was present anteriorly More than h lf of the posterior canal w ll wa absent A muco-purulent discharge was present nd granulation tissue filled the middle ear cavity

In April 1966, under 2% xylocaine-adrenalin anesthesia, the indicated tran meatal urgery wa carried ut (Lapid t & Brandow 1966) General anesthesia was then begun. Via th post uricular approach, the entire tympanic cleft surgery was perf rmed unsparingly The posterior canal wall w taken down and good visualization was obtained.

The malleus and part of the incus were identified and preserved. The reconstruction wa carried out a illustrated while a temporalis fascia free graft w used to repair the tympanic membrane defect It was placed upon gelfoam in th middle ear und r the previously prepared freshened free margin of the drum

Pathology w reported fragment of squ mous mucosa with hyper keratosi and fibrosi of submucosa fragment of bone nd keratin"

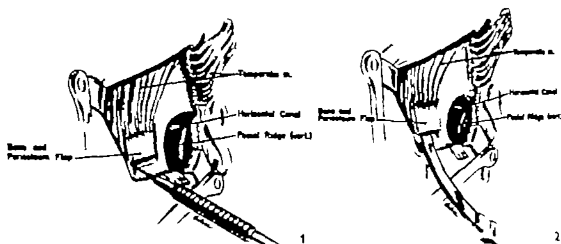


FIG 1 Burring out th outline of the pedicled bone-peri steum fragment.
FIG. 2. Separating the bon graft from the underlying spongiosa via a curved chisel

periosteum The rotation muscle-connective tissue flaps for the cavity which are attached above to the temporal region and below to the mastoid tip are now completed by an additional vertical and horizontal incision at the level of the zygomatic arch or lower if so desired The skin lining the "bowl" is elevated and excised except a small portion adjacent to the conchal cartilage which will give support to the new pedicled posterior canal wall *The entire cavity is carefully inspected and all the bone surface* is denuded of soft tissue and burred exenterating all disease A rotation pedicle bone-periosteal flap is planned from approximately the region where a horizontal line along the zygomatic arch meets a diagonal line 40 through the mastoid tip Here the temporal bone is sufficiently thick This flap is devised such that remaining attached to the periosteum is a fragment of outer cortical plus part spongy bone that will be advanced to form the new posterior canal wall (Figs 3 and 4) Burs are used to delineate the bone fragment (Fig 1) which is separated with a chisel (Fig 2) It is roughly designed in shape and size to replace the posterior canal defect Alternatively using alginate or self-curing acrylic resin the exact dimen sions can be ascertained and a replica pedicle constructed The latter has thus far not been done but is being planned for future cases.

The muscle flaps are placed against the posterior aspect of the newly created posterior canal wall approximated and sutured as described by Rambo A pedicle flap attached at the vascular strip area may be constructed from the canal skin and advanced posteriorly to line the newly created posterior canal wall To date we have not found it necessary since healing and epithelialization have occurred satisfactorily The external canal is packed with gelfoam while a penrose drain is inserted in the postauricular wound



Fig. 6. Postoperativ radiograph of Case 1 with contrast materi l filling xtern l canal.

The posterior canal wall is intact continuous and firm to blunt palpation with a probe There is a slight 1.5 mm indented area postero-inferiorly at the base of the newly created bony posterior canal wall However there is continuity of epithelium with drum and posterior canal wall across this area which i readily accessible for cleansing purpose should this at any time be necessary The tympanic membrane i intact but rather retracted and in part adherent The post operative radiograph of the external canal filled with contrast material is shown in Fig. 7

3 P J a 16-year-old male has had a draining right ear" since the age of 2 years with a hearing loss of 53 dB and 10 dB by air and bone conduc tion respectiv ly

In June 1962 a modified radical mastoidectomy (Type 3) myringoplasty was performed A revision tympanoplasty was carried out in March 1966 t which time a 90 perforation was reported. The middle ear was filled with lastic sponge and plit thicknes skin graft applied to cover the defecti e tympanic membrane Healing was reported as complete The pati nt however had a large ma toid cavity

In June 1966 under general anesthesia reconstruction of the posterior canal wall wa carried out using the pedicled temporal bone periosteum flap replacement. Post-operatively granulation developed in the external canal which resol ed further to local silvernitrate cautery The ear canal was lry wh n l st seen ten m nth post-operati ely nd the new posterior canal w ll w intact and epithelialized eliminating the pre-operative mastoid bowl

4 B J a 60-year-old Puerto Rican female at 58 years of age under went exci ion f an aneurysm f the left internal carotid artery During thi hospit lization she complained of pain in her right ear whi h was due t debris in a large mast id cavity F ventually she has since been well except for frequent visit to the ENT service for toilet of her mast id



Fig. 5 Photograph f hal line scar present after operati n.
Fig 7 Ca 2 illu trati n s in Fig 6

There was slight discharge from the ear for approximately three weeks for which acid-dehydrating solution of 4% boric acid in 70% alcohol was used as well as broadspectrum antibiotics and decongestants Further to this period, the ear has remained dry to date which is now one and a half years after operation The posterior canal wall is normal in appearance epithelialized and firm to palpation with a blunt probe The tympanic membrane is continuous and intact The post operative clinical photograph and radiograph of the external canal filled with contrast material is illustrated in Figs 5 and 6

2 A E an 18-year-old male has had a chronic running" ear right for 12 years At 15 years of age he underwent endaural mastoidectomy tympanoplasty and again at 16 years via post-auricular approach On examination a muco-purulent secretion filled the ear canal while the posterior half of the tympanic membrane was absent Thickened granulations replaced the defective drum and posterior canal wall defect The mean hearing loss by air and bone conduction was 67 and 10 dB respectively

In April 1966 an operation was performed as described in Case 1 The handle of malleus, which was markedly eroded was identified and removed The tissue from the middle ear was reported as "fibrous tissue and keratin debris"

The post-operative course was handled as in Case 1 and after three weeks the ear was "dry" and has remained so to the present which is 1 $^{1}/_{2}$ years.

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cavity The latter has been dry but her only complaint has been one of constant itching On examination an intact tympanic membrane was observed along with a large mastoid cavity containing dry epithelial debris.

In August 1966 a new bony posterior canal wall was created It was noted at time of operation that the handle of the malleus and long process of incus were present Tissue removed from the remaining mastoid cells was reported as desquamated epithelial cells and minute fragments of fibrous connective tissue and bone

Since operation the ear has remained dry which is now 18 months. There was slight over-correction of the new bony posterior canal wall which is in place and epithelialized There is a 1 5 mm undercut at the base of the canal wall but across this area the epithelium is continuous with canal skin and tympanic membrane The tympanic membrane is intact as in the pre-operative condition but slightly moist crusting tends to collect in the undercut area

COMMENTS

Review of the literature indicates that many modalities have been described for the elimination of the mastoid cavity" This would suggest that a uniformly accepted method is lacking It would appear that possibly avoiding to produce a mastoid cavity may well be considered Recreating a bony posterior canal for the defect in the external canal certainly appears reasonable to us This has been performed satisfactorily in four cases. Ten–eighteen months after operation all cases exhibit continuous, solid posterior canal walls at the site where they were placed at time of operation The slight undercuts at the base of the posterior canal walls in Cases 2 and 4 suggest that more accurate fashioning of the base of the bone periosteum flap to conform to the bed contous would eliminate these overhangs Unfortunately pre-operative radiographs with contrast material of the first two cases were not taken at the time

Three ears are dry and it is proposed to close the air-bone gaps in these patients at this stage

ZUSAMMENFASSUNG

Eine Operationsmethode wurde beschrieben die unter Ausnutzung eines Knochen Periost Lappens aus dem *Schlafenbein einen Canalis posterior* herstellt Wir fuhlen dass dies nicht nur von Vorteil in der Obliteration von Mastoidhöhlen ist sondern auch von Hilfe bei späterer Wiederherstellung chirurgie Die Methode wurde an vier Patienten mit gutem Erfolg benutzt Die beiden ersten hatten keine Mastoidhöhlen Während der Operation wegen chronischer Erkrankung der tympanischen Spalte wurden die Wände des Canalis posterior vollständig abgetragen und *in derselben Sitzung rekonstruiert F wird vorge-*schlagen dass diese Ergänzung der Ramboschen Technik unsere „Ohren Kruppel zu einem erheblichen Teil rehabilitieren könnte wie die präsentierten Fälle zeigen



FIG. 1. Ampulla of the guinea pig semicircular canal. The dark cell epitheli m (D) rest on connective tissue that cont i pigment. Crista (C) with sensory epithelium nd cupula.

either 1% osmium tetroxide, buffered with 0.1 M phosphate or 0.1 M cacodylate or 3 glutaraldehyde in 0.1 M cacodylate buffer followed by osmium tetroxide. The specimens were immersed in the fixati e for 1.5 hours. The specimens were dehydrated in ethanol and embedded in Epon plastic. The superi r horizontal and posterior ampullae were examined. A fine saw was used t di ide th e ampullae into several different blocks. These were mounted on Epon blanks for sectioning. Freehand sections were made for phase contrast light microscopy and LKB Ultrotome was used for making secti ns f r study with an RCA EMU 3G electron microscope. The sections w re t ined with saturated uranyl acetate in 50% ethanol.

For cyt chemical demonstration of adenosine triphosphatase activity ampullae wer fixed in 3 glutarald hyde in 0.1 M cacodylate buffer (pH 7 f r 30 m nutes. After washing in 0.1 M cacodylate buffer containing 8 ucr se tissues were reacted according to the procedure modified Wach t in Meisel (195) and post fixed in cold 1% osmium tetroxide in V r nal acet te buffer (pH .2). Details of thi procedure are described in previ u eprints (Nakai & Hilding, 1966 and 196).

RESULTS

Figu 1 illustrates the dark cell epithelium. It rests on connective tissue w th pigment nd blood vessels. It reaches from the base of the crista towards the place that the duct of the semicircular canal opens into the ampulla. It i separated from the perilymphatic space by a few loose layers f fibroblasts.

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VESTIBULAR ENDOLYMPH PRODUCING EPITHELIUM

Electron Microscopic Study of the Development and Histochemistry of the Dark Cells of the Crista ampullaris

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The dark cells of the ampullae have structural features that suggest that they may be engaged in the production of endolymph. They have a complicated folded membrane system resting on a basement membrane which resembles the cells of the distal convoluted tubules of the kidney and other sites of fluid secretion ATP ase can be histochemically demonstrated on the surface of these folded membranes. The dark cells develop in stages from a simple cuboidal epithelium during maturation of the inner ear

Dark cells are found in the lining of each ampulla near the base of the crista extending towards the openings of the semicircular canal Kimura *et al* (1964) demonstrated that electron microscopy of this epithelium suggested that it produced endolymph There are different non sensory cell types in the vestibular labyrinth epithelium including rather plain cuboidal cells of the planum semilunatum and transitional cells which these authors also discuss Bairati & Iurato (1960) and Dohlman (1964 and 1965) performed an electron microscopic study of secretory cells of the labyrinth.

MATERIALS AND METHODS

Specimens were studied from 9 rabbit embryos varying between 22 and 30 days 3 newborn rabbits, 5 adult mice 3 adult guinea pigs and 3 adult squirrel monkeys.

As quickly after death as possible the vestibular structures were placed in fixative solution after opening the round window lifting the stapes, and enlarging the oval window The utricle and semicircular canals were opened adjacent to the ampullae to facilitate the penetration of the fixative The ampullae were dissected out in fixative solution The fixatives used were

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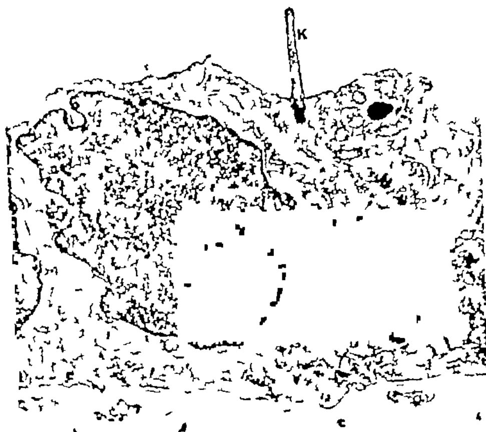


Fig. 4. T t -(l day t g d rk cell epithell m A ingle kinocili m (K) rises from ach cell d ing these ea lier t ges of dev lopment At this st ge f lding has bega (the basal regio nd the interdigit tion bet een neighboring cell ha progressed The paces bet ee cell d t the base re beet like l the gl t raid hyde-fixed tissue 18,000

In early stages, uch a the 22 day stage of the rabbit fetus, this epi th lium i a simple cuboi lal layer There i a tight jun ti n between n ighboring cell along the end lymphatic surface and there are a few interdigitatio n between cells. The nuclei are large enough to occupy much of each cell v lume Mitochondria and end plasmi reticulum are found

Fig. 2 Fut re dark cell epithell m Twent -t da rabbit fetus. At this stage there i regul row of boid l cells ith larg ucl i 6300

Fig. 3. Tw ty t day stage higher mag ification. The proces of i terdigit ti be t een djacent cell has just begu (arrow) but the basal fold ha not formed yet. At ll st ges basement membrane (BM) i present bene th thi layer of cell Osmic acid fi tion. 37,000





Fig. 7. Adult dark cell epithelium, basal portion. The surface area of these cells is enormously increased by the folded cell processes of this region. Vesicle rows are seen. A basement membrane (BM) is present. Pigment granules (P). Adult mouse, osmium fixation. × 21,000.

in moderate abundance in the cytoplasm (Fig. 2). A basement membrane is found beneath the layer of cells (Fig. 3).

At 25 days interdigitation begins to form between adjacent cells. A few microvilli persist at this stage but will disappear later. Each cell has a single kinocilium with a basal body and the ordinary 9 + 2 pattern of microtubules (Fig. 4).

Fig. 5. Twenty-seven day stage. A complicated pattern of folded cell-processes has formed. × 6000.

Fig. 6. Twenty-seven day stage, higher magnification of basal portion of cells. Long rows of vesicles (arrows) run parallel to some spaces. In adult the vesicle rows are replaced by continuous spaces. Osmic acid fixed rabbit fetus. × 16,000.


5
6

ATP-ase activity can be demonstrated histochemically on the surface of these folded membranes as illustrated in Fig. 8. The probable significance of ATP-ase distribution was discussed in our earlier papers about its cochlear distribution (Nakai & Hilding, 1966 and 1967). Although there is always legitimate objection to over reliance on histochemical data, staining of these membranes is additional evidence that fluid transport is occurring. Notice that the spaces are substantially larger between cell processes in the illustrated specimen. This may be due to the different way these specimen were treated or be a species variation, but might also reflect a different physiological state.

DISCUSSION

Vestibular dark cell epithelium resembles the stria vascularis in a simpler form. Each has a system of complicated folded membranes in the deeper zone and vesicles in the region next to endolymph. Neither has microvilli. However the vestibular epithelium has a more primitive arrangement of only a single layer of cells, whereas the stria vascularis epithelium has three layers. As the cochlea evolved the two inner layers of the stria epithelium were added from underlying mesodermal tissue. Perhaps the more complicated structure of the stria is needed to maintain the large DC resting potential of scala media (Békésy 1952). According to several experiments, the DC potential of vestibular endolymph is much smaller (Davis, 1960). However the more complicated form of stria may represent a more efficient means of producing endolymph.

In osmium fixed adult vestibular dark cell epithelium the zone next to the basement membrane has a richly folded membrane system with continuous cleft like spaces. Our 27 day fetal tissue treated in the same way shows rows of vesicles that probably represent sheets of tubes. In ciliary epithelium from the rabbit eye similar rows of vesicles are an artifact due to osmium fixation that resolve to sheets of folded membranes when glutaraldehyde or formaldehyde are used (Tormey 1964 and 1966; Matsusaka, 1967). We were unable to obtain satisfactory aldehyde fixation at the 27 day stage to determine whether these results could be reproduced. Notice that osmium fixation does not produce this type of artifact in adult specimens.

The passageway between folded lateral cell processes probably is an important feature of this epithelium. There is an intimate relation of fluid passing through this large area of cell membrane. The gall ladder is lined with cells that vary the dimension of this type of space depending on their physiological state.

Gradually we have begun to consider endolymph production as a process of fluid and electrolytes passing between cells rather than through them. However we are still far from a satisfactory theory to explain its production because we lack so many important facts about sodium and potassium

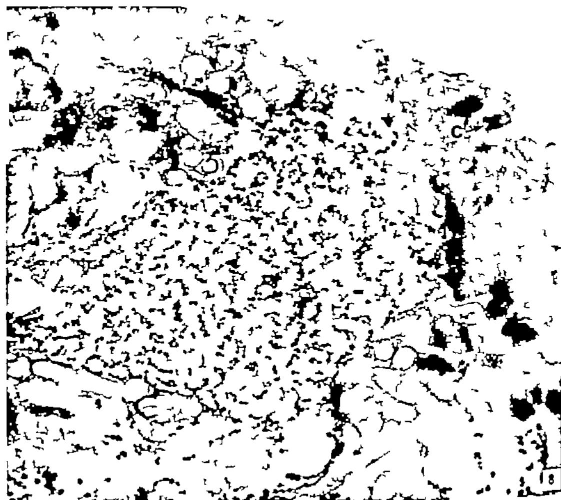


FIG. 8 The bl ck granul s are a lead precipit t whi h formed as a result f histo- h mic l treatment fo th dem nstrati n f ATP ase Th surface of the f lded cell proc ses is rea tl\ In the z n near endolymph th re are a \esi les A pair of centri les (C) 32,000

In the 27 days stage of the rabbit fetus, about 3 days before birth complicated interfolding between adjacent cells was seen as illustrated in Figs 5 and 6 An interesting feature at this stage are the rows of vesicles that stream through the cytoplasm which may be osmic acid fixation artifacts

In the adult a complicated system of folded membranes develops in the basal portion of the dark cells (Fig 7) The outer surface of adjacent processes nerve seem to approach closer than 100 A regardless of their convolutions Perhaps they have an outer layer that is invisible to the electron beam Apparently depending on the activity of a group of cells, the space between these cell processes varies from the uniform minimum to large spaces This sort of variation has been correlated with physiological state of the epithelium of the gallbladder (Kaye *et al* 1966) In the apical region near the endolymph these cells have no microvilli but they do have a large number of vesicles of various sizes

ATP-ase activity can be demonstrated histochemically on the surface of these folded membranes as illustrated in Fig 8. The probable significance of ATP-ase distribution was discussed in our earlier papers about its cochlear distribution (Nakai & Hilding, 1966 and 1967) Although there is always legitimate objection to over reliance on histochemical data, staining of these membranes is additional evidence that fluid transport is occurring Notice that the spaces are substantially larger between cell processes in the illustrated specimen. This may be due to the different way these specimens were treated or be a species variation, but might also reflect a different physiological state

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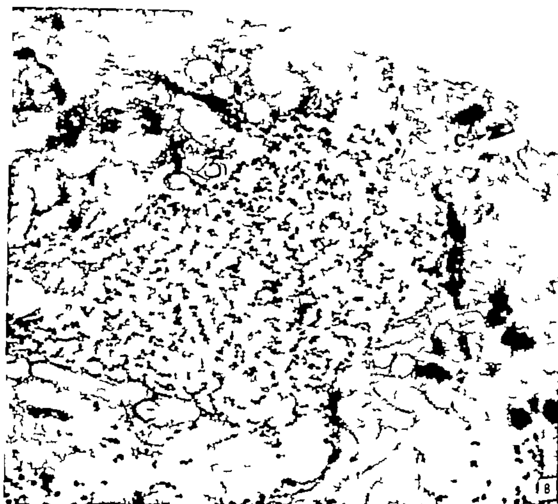


Fig. 8. Th black granules are a l d precipitat whi h f rmed result f histoch mi al tre tm nt fo the d mon tration of ATPase Th urface f the f lded cell *processes is re tl In th zon n e d lymph th re are vesi les A pai of centriol s (C) 32,000*

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THE INNER EAR IN PENDRED'S SYNDROME

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Histological examination of the temporal bones from a patient with confirmed Pendred's syndrome revealed bilateral Mondini type malformation of the inner ear.

In 1896 Vaughan Pendred, a British general practitioner, described two sisters who were deaf mute and had severe goitre. In the course of time a number of similar cases have been published in which the familial occurrence indicated a more than chance coincidence of deafness and goitre. It was not until 1958, when Morgan & Trotter demonstrated that the goitre was due to a recently described inborn error of metabolism in the iodine metabolism of the thyroid, that the tracing of these cases really gathered speed. Fraser in 1965 collected data on 223 cases of Pendred's syndrome, which is now generally accepted as the eponym of the disease. Fraser estimated that this recessive inherited disease occurred in about 1/13,000 of the British population.

While a good deal is known about the pathology and pathophysiology of the disease as far as the thyroid gland is concerned, histological examination of the hearing organ does not appear to have been reported previously. Audiometric tests show in the great majority of cases, severe hearing loss, especially in respect to the high frequencies.

Nilsson *et al.* (1964) demonstrated positive recruitment in 4 out of 12 cases. An abnormal vestibular function as well as other studies have indicated an inner ear involvement, but the nature of this lesion has so far been unknown. Various theories have been advanced in the endeavour to explain the hearing defect by the thyroid changes or by a common humoral pathogenetic factor.

Case Report

The present patient was a 60 year-old man who had been born deaf and who had had a tendency to goitre from the age of 25. His paternal uncle was deaf but did not have goitre, but a maternal aunt with normal hearing had goitre. From his earliest childhood the patient had suffered from a severe hearing impairment and he had attended several state schools for the deaf to have speech instruction. There are no data concerning an aural disease. Otoscopy has not disclosed any abnormality. Unfortunately no

flux It seems likely that the simpler vestibular dark cell epithelium may provide a better tissue to study endolymph production than the stria vascularis

ZUSAMMENFASSUNG

Die dunklen Zellen der Ampullae haben strukturelle Eigenschaften welche den Gedanken nahelegen dass sie an der Produktion von Endolymphe teilnehmen. Diese Zellen haben ein kompliziertes, vielfach gefaltetes Membransystem, welches auf einer Basalmembran ruht ähnlich den distalen konvolierten Tubuli der Niere ATPase kann histochemisch an der Oberfläche dieser gefalteten Membranen demonstriert werden Die dunklen Zellen entwickeln sich stadienweise von einfachem kubischem Epithel während der Reifung des Innenohres.

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Fig. 2. Basal turn of the left cochlea, showing ... trophic organ of Corti, absence of the tectorial membrane, dilated Reissner's membrane and complete atrophy of the nerves ... the lamina spiralis. In the upper left-hand corner can be seen ossification in the ... connective tissue.

Since descriptions of autonomous growth in Pendred's syndrome had been found in the literature, the second strumectomy was carried out. 25 g of tissue was removed. This specimen was not examined microscopically but stored deep frozen for a possible subsequent enzyme determination. Replacement therapy with thyroid was instituted. Nevertheless, the goitre again recurred and in the third strumectomy done 6 months later, 20 g tissue was removed, still from the right side. The histological diagnosis was nodular and adenomatous goitre. The histological appearances corresponded to what has been described in the literature as being characteristic of Pendred's syndrome.

The thyroid tissue was split up into numerous connective-tissue nodules varying in size. In these strands there were occasional clusters of lymphocytes, but on the whole they were poor in cells. In most areas the follicles were small to medium-sized, regular round with slightly varying, but usually ample colloid content. The epithelial cells were medium-sized, cuboid, fairly uniform. Here and there the nuclei were somewhat enlarged, hyperchromatic and a bit angular, but there were no mitoses. In the capsule there were in several places islets of thyroid tissue in which the follicles were particularly small and rather more irregular, but there was no penetration of the capsule and no invasion of vessels.



Fig. 1 Left t mporal bone showing defective development of the cochlea which has onl 2 turns, an u der-d vel ped modi lus, nd connecti e-tissue formation in th a-cula

audiometry or other estimation of the hearing was available but from in formation received from the deaf schools it may be learnt that the patient was totally deaf or at least suffered from very severe hardness of hearing From about the age of 25 he exhibited goitre which appeared to be growing slowly

At the age of 40 he had his first strumectomy At that time he had moderate symptoms of tracheal compression but no objective or anamnestic signs of thyrotoxicosis The operation revealed a firm goitre weighing 2/0 g The histological diagnosis was colloid nodular goitre The histological report mentions some follicular atypia and subsequent revision of the preparations showed the changes which will be described below

At 58 years of age the patient was admitted to the City and County Hospital Nyborg with arteriosclerotic heart disease A goitre was observed which the patient had noticed for the past 3 months The PBI was 1.2 μg and the serum cholesterol 253 mg 100 ml At the time the pati nt was not interested in an operation

When he was 60 the recurrent goitre had progressed to the size of a hen s egg and it was situated on the right of the cricoid cartilage Now the enzyme defect was demonstrated when he was re admitted to the Ny borg Hospital as an I^{131} test showed normal values, while a perchlorate test showed a 28% fall in one hour For the test he had been given a maximum of 15×10^{-4} mg iodine and the PBI was 1 0 μg/100 ml The patient did not give an impression of myxoedema and his B M R was −14 triiodothyronine test 92% and serum cholesterol 324 mg 100 ml

other hand, is a recessive character which accords with its apparently sporadic occurrence in our case. The named developmental anomaly might be explained by an arrest in cochlear development around the 6th foetal week. It is not possible to demonstrate a relationship to the thyroid defect. Therefore as previously Pendred's syndrome has to be ascribed to two facets of or a defect of a heterophenic gene.

ACKNOWLEDGMENT

Thanks are due I. W. Kiær, M.D., Pathologist to the Central Hospital, Svendborg, for the microscopic examination of the thyroid tissue and for supplying the temporal bones.

ZUSAMMENFASSUNG

Die histologische Untersuchung der Schläfenbeine bei einem Patienten mit Pendred-Syndrom zeigte eine doppelseitige Missbildung des inneren Ohres vom Typ Mondini's.

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was also normal The semicircular canals were slightly dilated The aqueduct of the vestibule was shorter and of far wider calibre than normal There was also dilatation of the endolymphatic duct and sac (Fig 4) In the vestibule too there were increased quantities of periotic connective tissue with ossification along the endosteum of the labyrinthine wall

DISCUSSION

In patients with Pendred s syndrome the iodine metabolism in the thyroid is defective in the stage where after having been trapped by the thyroid, inorganic iodine is incorporated in the thyroglobulin molecule where it is bound in an organic form to tyrosyl radicals This particular defect in the thyroxine synthesis is fairly easy to detect owing to the ability of certain inorganic anions (e g perchlorate or thiocynate) to release inorganic iodine from the thyroid gland In normal glands the organic incorporation is very rapid and only little inorganic iodine is present Therefore the named ions do not affect the counting rate over the thyroid after administration of radioactive iodine In patients with Pendred s syndrome, on the other hand, administration of radioactive iodine is followed by a dramatic fall

The perchlorate test is positive in certain cases of Hashimoto s thyroiditis, and the administration of large quantities of iodine or thiouracil may show a positive response

Thiouracil like preparations were not administered to our patient and the total dose of iodine was, as already mentioned very small Moreover the low PBI at the time of the test rules out iodine contamination An autoimmune disorder of the thyroid gland is excluded by the histological structure of the goitre and by the absence of serum antibodies

The bilateral developmental arrest in the labyrinth is of the Mondini type The histological appearances correspond rather accurately to Ormerod s (1960) and Altmann s (1965) present-day descriptions of this developmental anomaly which had been described by Mondini as early as 1791

Apart from the malformation, however there were also signs of a more recent secondary degeneration, such as atrophy of the organ of Corti and of the tectorial membrane hydrops connective-tissue formation in the saccule and utricle and an increased amount of periotic connective tissue with ossification along the labyrinthine endosteum

It cannot be decided whether both types of changes or only one is a consequence of the enzyme defect of Pendred s syndrome Since however inner-ear defects of the Mondini type can often be diagnosed by Polytome tomography of the inner ear (Jensen 1967) part of this problem can be solved by systematic tomography of all patients with confirmed Pendred s syndrome

As a rule the Mondini defect has been found in patients whose deafness is characterized as a dominant inherited trait Pendred s syndrome on the

Further evidence that the perilymph is not a simple filtration product of either CSF or serum, was obtained from enzyme analyses. Thus unspecific esterase patterns in the perilymph differed sufficiently from the CSF and serum patterns to exclude their presence in the perilymph without some extra mechanism. Similarly the presence of LDH_4 and LDH_5 bands in stronger concentration in the perilymph and endolymph than in CSF or serum pointed clearly towards some active mechanism playing a part in the production of some of the components of cochlear fluids. It cannot however be seriously questioned that the perilymph proper with its main protein components derives from some source other than the CSF or serum, although some of its components may originate from the nervous tissue or from active cellular secretion.

One way to clarify this would be to identify in the perilymph a substance that is identical with the corresponding substance in CSF for instance but differs in some respect from the same substance in serum. The inorganic ions obviously are not helpful, nor does the different composition of the enzymes in the three fluids contribute to make them useful in this respect. We have focused our attention on albumin being a composite protein, it may show enough characteristics enabling one to identify two of the three albumins as identical and one as different.

We have pointed out earlier that, in immunoelectrophoresis the perilymph albumin is antigenic similarly as that of CSF or serum albumins. However owing to slightly different composition the mobility of serum and CSF albumin is not exactly the same (Löwenthal *et al.* 1960). The difference is so slight as to render its detection impossible in disc electrophoresis, but it can be demonstrated by studying the relative mobility of the two albumins in an electrophoretic field. Having the perilymph and endolymph albumins in these experiments as running partners it may then be possible to disclose new information on the origin of labyrinthine fluids.

METHODS

The electrophoretic analyses were performed by agar gel electrophoresis using a modified method of Wieme (1965). The modifications were concerned with the size of agar electrophoresis plates with the junction between plate and agar blocks, and with application of samples and reference substances.

In our preliminary attempts, microscope slides (25 mm × 6 mm) were used. However the width of the slides was found to be too small to run three samples (serum, CSF and perilymph or endolymph) on the plate. Distortion of pherograms, such as curving of bands, was observed near the long sides of the plates. Therefore, the conventional microscope slides were replaced by slides with a width of 40 mm. It was also necessary to provide a homogenous junction between the plates and the agar blocks through the width of the plate. This was accomplished by agar slabs (4 × 40 ×

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THE ORIGIN OF PERILYMPH ALBUMIN

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Results are presented of analyses of serum, CSF perilymph and endolymph electrophoretic mobilities in 24 cadaver ears. On an average perilymph and CSF albumin had identical mobility whereas the mobility index of serum albumin was clearly slower than the other two It is concluded that perilymph albumin as a rule has its source in the CSF space and is apparently transported through the cochlear or vestibular aqueduct or along the eighth nerve through foramina at the internal acoustic meatus.

In two earlier papers (Palva & Raunio 1967 *a* and *b*) we have reviewed the present knowledge of the composition of labyrinthine fluids. Conventional and micro disc electrophoretic analyses of perilymph and utricular endolymph from human cadaver ears led us to the conclusion that both fluids contain a constant strong band of albumin and an equally constant, but much weaker band of fast prealbumin In addition two slower and much weaker prealbumin bands were also found in the perilymph In the endolymph these latter bands appeared irregularly the relatively poor resolution power of the disc micro method at the anodic end made conclusions as to their regular appearance in endolymph to some extent uncertain.

The other protein bands nearer the cathodic end appearing regularly in both perilymph and endolymph runs were apparently due to dissolved hemoglobin and to various other components derived from the capillaries after death

Consequently the earlier results of Chevance *et al* (1960) demonstrating 13 different protein components of the perilymph were considered as artefact, their method of microscopic examination providing no control of contamination with dissolved hemoglobin In all essentials our findings agree with the results of Beck & Holz (1966) indicating that the perilymph contains only a few protein bands

Our (Palva & Raunio 1967 *a* and *b*) comparative analyses of cerebrospinal fluid (CSF) serum and perilymph showed that the first two contained sufficient albumin and fast prealbumin to be a possible source of perilymph However the weak slower prealbumins present in perilymph were absent from these two possible precursor fluids Electrophoretic analysis of human brain tissue and of acoustic nerve on the other hand showed a band moving identically with the faster of the weak prealbumin bands in both tissues

The following conditions were employed during electrophoresis field strength 25 V/cm, temperature of petroleum-ether (b.p 30 –40) +12 C, duration of electrophoretic run 30 min. 1% Special Agar Noble (Difco) made in veronal buffer pH 8.4 ionic strength 0.05 was used in plates and agar blocks.

In the Wieme method of determination of relative mobilities, the reference substances (albumin macrodex and transferrin) are run parallel to the sample on the same plate To create a system in which reference substances are run along the same migration axis as the sample substance we mixed transferrin and dextran with the sample By this technique exactly same conditions for electrophoretic separation of reference substances and albumin are provided. After electrophoresis, the plates were fixed in a bath containing ethanol 70 vol acetic acid 5 vol., and distilled water to 100 vol to precipitate the dextran. As soon as this showed up as an opaque band, a cut was made at the line corresponding with the middle of the band The plates were then dried and stained with Amidoblack.

Migration distances were measured by scanning the plates in a densitometer and locating the fractions by their maximal optical density The distance between transferrin and dextran bands was used as a unit By dividing the distance between albumin and dextran with this unit the relative mobilities of albumins were calculated. The mobilities were also calculated by using the distance dextran-serum albumin and this distance was given the unit value of 1000 (Fig. 2)

It is known that albumin mobilities are related to the concentration of albumin (Wieme 1964) Therefore, the concentrations of albumins to be compared wer adjusted to approximately the same level With this objective serum was diluted to 1 10 and in some cases CSF was concentrated 5 to 10 times. Th concentrations of reference substances were as follows albumin (Behringwerke) 5 mg/ml transferrin (Behringwerke) 5 mg/ml Dextran (Pharmacia, Uppsala) 5 mg/ml. The method for obtaining and storing the perilymph and utricular endolymph samples in cad ver ears has been described earlier In this study samples of cochlear endolymph were also used After taking the perilymph and utricular endolymph samples, bon was removed over the basal coil of the cochlea, the round window membrane removed and the perilymph space aspirated dry with a fine-caliber needl aspirator A very thin gla s pipette was then introduced into the cochlear d ct and fluid collected by capillary force The amount obtained was generally 1 to 2 µl. Cerebrospinal fluid was obtained by lumbar puncture and aspiration serum was aspirated *from the large* thoracic veins.

RESULTS

Perilymph samples were obtained from 24 ears. The relative mobilities of the 24 perilymph albumin bands relative to those of serum and CSF as determined by using transferrin-dextran distance as a unit are presented

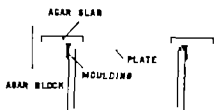


Fig 1

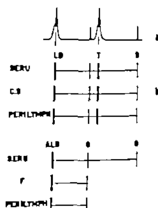


Fig 2.

Fig 1 The figure shows the arrangement fo the junction between the lectrophoresis plate and agar blocks in the "Vitatron" Agar Electrophoresis tank.

Fig 2. Calculation principles for measuring relative mobilities. (a) Scheme showing the marking of the maximal optical densities on densitometric trace (b) th relative mobilities were calculated from

$$m \text{ alb} - \text{serum} = \frac{(\text{Alb}_{\text{serum}} - D)}{(T - D)}$$

$$m_r \text{ alb} - \text{CSF} = \frac{(\text{Alb}_{\text{CSF}} - D)}{(T - D_2)}$$

$$m \text{ alb} - \text{perilymph} = \frac{(\text{Alb}_{\text{peri}} - D)}{(T - D)}$$

or (c)

$$m \text{ alb} - \text{CSF} = \frac{(\text{Alb}_{\text{CSF}} - O) + (O - D)}{(\text{Alb}_{\text{serum}} - D)}$$

$$m \text{ alb} - \text{perilymph} = \frac{(\text{Alb}_{\text{peri}} - O_2) + (O_1 - D)}{(\text{Alb}_{\text{serum}} - D)}$$

Alb, lbumin D d xtra T transf rrin O st rt

40 mm) prepared at the same time as the plates The upper surfaces of the agar blocks and the plates were brought to the same level with the aid of two plexiglass mouldings These mouldings also helped to place the plates in the apparatus in exactly the same place for each run (Fig 1)

Application of the samples was performed with a blade (width 4 mm) mounted on a perspex support 1 μl of sample was pipeted on to each of the applicators and the edges were then gently pushed into the agar gel to make three well aligned cuts down to the glass. By this technique a good starting line was provided which never opened to a gap during the electrophoretic run and subsequent manipulations of the agar plate Drying of the slit with a piece of filter paper before sample application was not necessary

difference was observed using the transferrin-dextran distance unit the mean figure for serum albumin being 2.085 and for CSF 2.122 A single specimen (Table 1) may not always show differences in albumin mobility but on an average the CSF albumin moves faster than serum albumin The individual results in Table 1 suggest further that the numerical values in any of vertical columns cannot as such be used as indicators of mobility the difference between the three samples run on the same plate are much more useful to thi purpose Even if the runs are made under as identical conditions as possible there are factors, hard to control that may cause differences. These include the adjustment of serum, CSF and cochlear fluid albumin concentrations to identical values, and the possibility of there being some slight differences in agar thickness in different runs. A further ource of inconsistency may be in the mechanical marking of dextran (de Boer *et al* 196)

All the three albumin to be compared are contaminated with hemoglobin and even though the serum albumin has a larger supply of hemoglobin than the other two, the fact that albumin becomes saturated and c n carry along a limited amount of hemoglobin only does argue in favor of the conditions being identical in the case of all three fluids. The result indicate that as an average perilymph and CSF albumin have similar mobility and that both mo e in an electrophoretic field faster than does serum albumin This finding clearly points toward CSF being a ource of perilymph albumin The question whether the cochlear or vestibular aqueduct or the acou tic nerve canal functions as a pathway for fluid transport cannot be answered for the time being

In the series of endolymph runs, some show no difference between serum and endolymph albumin and some utricular and cochlear endolymph samples seem t contain albumin that i faster than serum albumin and identical in mobility to CSF lbumin It must be kept in mind that some samples may be cont minated with perilymph and are thus not representativ of pure endolymph Some samples may also have contained cellular element from the end-organ and their effect on albumin m bility is un known t present

ZUSAMMENFASSUNG

A alysen über d lektrophoretische Beweglichk it von Albumin wurden *i* 21 Lei hen bren für Serum, Zerebrospinalflüssigkeit, Perilymphe und Endolymphe durchgeführt. Man f nd da das Albumin von der Perilymphe und der Zerebrospin lflüssigk it ei identische Beweglichkeit hatt und das das Serumalbumin sich langsamer bewegt Danach zu schliessen h t das *Albumin der Perilymphe* seinen Ursprung in der *Zerebrospinalflüssigkeit, deren Transport* entweder durch den Aqueductus cochlea oder *estibuli oder durch de Meatus* acoustien interna d Nervenfasern *entlang in den perilymphatischen Raum* erfolgt

between serum and perilymph this increases to 99 per cent while CSF and perilymph albumin mobilities show no difference statistically

The calculations of relative mobilities made using the distance between albumin and dextran as a reference unit gave the following average results CSF 1 0079 and perilymph 1 0074 with S D s of 0 019 and 0 015 respectively Thus statistically there is no difference between CSF and perilymph. Between serum albumin on one hand and CSF and perilymph on the other there is clear mobility difference (95 per cent probability)

While the general trend in the table is clear there are some individual results in which the three values are essentially the same and some in which the perilymph albumin moves slightly faster than either of th suspected mother fluid albumins (Fig 3) The three control runs in the ears marked with an asterisk ( ) show although some numerical values differ the same difference between mobilities as was noted in the ordinary runs In two ears 9 successive control runs were made in both in these perilymph and CSF albumin consistently moved slightly faster than serum albumin Another control run was made by testing 10 plates with purified albumin in all three wells the average results showed no statistical difference and location of the migration axis at the electrophoresis plate thus apparently had no effect on the result.

Since our earlier results (Palva & Raunio 1967 *a* and *b*) showed that perilymph is contaminated with hemoglobin which in turn becomes absorbed by the proteins control runs were made to see if this affects the mobility For this purpose whole blood was withdrawn from 10 patients, the samples were centrifuged and the cells separated Serum from each sample was divided into two parts one was diluted with distilled water to 1 10 of the original and the other to same concentration using cell hemolysate from the same sample Both sera were kept in a refrigerator for one week *to effect the absorption of hemoglobin by albumin Electrophoretic* mobility was then determined the average result for the water-diluted samples of 10 was 0 982 and for the hemolysate-diluted samples 0 972. Hemoglobinalbumin complex thus made the mobility slightly slower

Altogether 18 endolymph samples were analysed, 10 from the utricle and 8 from the basal coil of the cochlea The endolymph albumin, in half of the cases of both groups, had a faster mobility than serum albumin and comparable to CSF In the remaining cases endolymph and serum albumin showed identical mobility CSF albumin also joined this group in five cases but in four cases it moved at a slightly faster rate than the other two

DISCUSSION

The conclusion of Löwenthal *et al* (1960) concerning the difference in mobility between serum and CSF is confirmed by our results While their average values for serum were 0 986 and for CSF 1 006 ours for CSF was 1 0079 when the *serum albumin was given the unit value of 1 000* Similar

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VESTIBULAR RESPONSES FOLLOWING HIGH VELOCITY ROTATION

Normal Material

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Nine persons were submitted to rotation for various periods of time in a hand operated rotating chair at velocities of about 280°/sec and with very abrupt starts and stops. The purpose has been to establish normal material with which a group of ballet dancers can be compared in order to ascertain the eventual existence of occupation-induced habituation. Results were recorded by electronystagmography and telemetry techniques. Slow phase velocity of eye movement in the early postrotation period was used to score the responses.

Certain professions involve exposure to extreme degrees of vestibular stimulation, the consequences of which the individual must learn to control through intense training. Such occupation induces habituation which has been the object of many studies, usually by means of recording the vestibular response to some standard clinical test. These tests often reveal very little or only doubtful evidence of an objective response decrement. Thus the question arises if habituation is of specific character and only clearly demonstrable if the test situation closely imitates the professional task. Such demands will ordinarily make it difficult to obtain normal material with which the professional group can be compared. In a thorough study *Collins* (1966) submitted professional figure skaters to a whole battery of vestibular tests, including also pirouettes in the laboratory and on ice performances. He found that vigorous nystagmus and turning sensations occurred following spins, when visual fixation was not permitted, and suggested that ability to exert some visual control over the effects of vestibular stimulation may account for the previous findings of *Mowrer* (1934) and *McCabe* (1960) who reported opposite results. He stated that possibly nystagmus responses of the skaters in total darkness may differ in some ways, on the average, from responses of ordinary subjects, but a larger sample of skaters, quantification of nystagmus and statistical comparison with a non-skater group would be required to establish these relations.

Having had the opportunity to examine a group of dancers from The

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VESTIBULAR RESPONSES FOLLOWING HIGH VELOCITY ROTATION

Normal Material

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From the University E.N.T.-Clinic, Rigshospital, Copenhagen, Denmark

Nine persons were submitted to rotation for various periods of time in a hand operated rotating chair at velocities of about 280°/sec and with very abrupt starts and stops. The purpose has been to establish normal material with which a group of ballet dancers can be compared in order to ascertain the eventual existence of occupation-induced habituation. Results were recorded by electronystagmography and telemetry technique. Slow phase velocity of eye movements in the early postrotation period was used to score the responses.

Certain professions involve exposure to extreme degrees of vestibular stimulation the consequences of which the individual must learn to control through intense training. Such occupation induces habituation which has been the object of many studies, usually by means of recording the vestibular response to some standard clinical test. These tests often reveal very little or only doubtful evidence of an objective response decrement. Thus the question arises if habituation is of specific character and only clearly demonstrable if the test situation closely imitates the professional task. Such demands will ordinarily make it difficult to obtain normal material with which the professional group can be compared. In a thorough study Collins (1968) submitted professional figure skaters to a whole battery of vestibular tests, including also pirouettes in the laboratory and on ice performances. He found that vigorous nystagmus and turning sensations occurred following spins, when visual fixation was not permitted, and suggested that ability to exert some visual control over the effects of vestibular stimulation may account for the previous findings of Mowrer (1934) and McCabe (1960) who reported opposite results. He stated that possibly nystagmus responses of the skaters in total darkness may differ in some ways, on the average, from responses of ordinary subjects, but a larger sample of skaters, quantification of nystagmus and statistical comparison with a non-skater group would be required to establish these relations.

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F a. 1 Prima *ball rin* *K rst n Sim n* d preml d \en *H nni g* Kron tam *l* *Swan Lal* (Th Roy l Ballet, Copenhagen)

Royal Danish Ballet we felt the same need for having a normal material to compare our results with

For establishing such normal material two parameters are of main im portance the velocity of rotation and the period during which the subject is rotated at constant velocity Both parameters should be approximated as closely as possible to the normal dancing situation Starts and stops in dancing are very abrupt and there is little meaning in attempts to quantify acceleration and deceleration in degrees per sec^2 An exact evaluation is

further complicated by ballet dancers use of the so-called spotting technique This problem will be dicussed in a future communication Peak velocity during pirouettes for ballet dancers is a little more than one rotation per sec. Thus *Swan Lake* demands the performance of 32 successive rotations (fouettés) in the course of about 24 sec (Fig 1) The duration of rotation is naturally highly variable, but as just mentioned the perrotatory period may be quite extended The degree of nystagmus resulting from axial rotation is determined by the mechanical behaviour of the cupula in the lateral semicircular canal (Dohlman, 1935) and the nystagmus intensity corresponds to th magnitude of cupula deviation at any time. Because of inertia the cupula will deviate during an acceleration If rotation is maintained at constant velocity elastic forces will make it return to its normal position in the course of about 20 sec during which period the nystagmus gradually subsides. At deceleration the same course of events is repeated just in opposite direction and there should be a postrotation nystagmus with a duration of about 20 sec. A sudden turn of the head will cause a cupula deflection but the immediate stop makes it return to normal position and there will be no nystagmus following the movement. Thus from a theoretical standpoint the postrotational nystagmus is determined equally by the duration of the perrotatory period and by the velocity

OWN INVESTIGATIONS

Motor dri en rotating chai s have a maximum elocity of 200 /sec and furthermore all change of speed is rather slow when compared to natural mov m nts. We therefore decided to use an old fashioned Bárány rotating chair which we found it possible to run at a velocity around 280 /sec, when the test subject is sitting in the precise axial position This velocity is reached at the beginning of the second turn Deceleration to full stop could be achieved within on half turn and less than one half sec, yielding an estimated decel ration of around 700 /sec²

In preliminary tests with the dancer group this type of otation was found acceptable and, what is important, the dancers could employ their su l spotting technique without any difficulties.

In rder to establish a proper test procedure it was decided to measure systematically th degree of nystagmus following rotation at various lengths of tim The test mat rial was 3 nurses, 3 female secretaries, and 3 doctors. The age ranged from 22 to 47 years with an average of 33 years. They were selected t random in the department and were all unexperienced with regard to such e periments. Rotations were performed clockwise according to the following schedule 3, 6, 9 12 9 6 and 3 rotations. For the purpose of judging the eventual habitu tion incurred through this succession of unilateral stimulations 4 subjects were rotated 9 times in the counter lockwise direction t the end of th procedure.

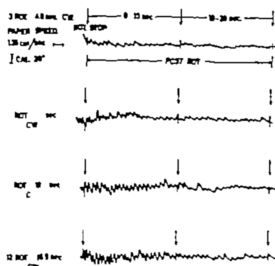


FIG 2. Example of lectronystagmographic response following increasing nmber of rotations.

The duration of each rotation period was measured by stop-watch. Variations for each set of tests were kept within one sec

The subjects had closed eyes during the whole of each test run and were instructed carefully about the importance of keeping the eyes in a midline position during the recording. By observation of the closed eye-lid it was easy to certify that these instructions were followed

Eye movements were recorded by electronystagmography (Fig 2) with electrodes taped by the outer canthi and an indifferent electrode on the forehead The signal was amplified and transferred to the recorder by means of F M telemetry technique The amplifier and F.M transmitter together were of small dimensions and could be strapped to the chest without impeding free natural movements in any way The use of this transmission technique reduced the time constant of recordings to almost one sec Our equipment has been described in further detail by Osterhammel & Pettersen (1967)

RESULTS

All 9 subjects experienced considerable vertigo when exposed to more than 3 rotations Two became nauseated after the 9 and 12 rotation test respectively so that the session had to be discontinued No one has suffered any lasting ill effects. For scoring of results is was evident that nystagmus duration would be of little value Many subjects showed typical beats even after several minutes and the end point was not well defined Furthermore there appeared to be no correlation between such long lasting reactions and the intensity of the early response

The most consistent parameter was found to be the slow phase eye displacement immediately after the rotation Fig 3 shows slow phase velocity

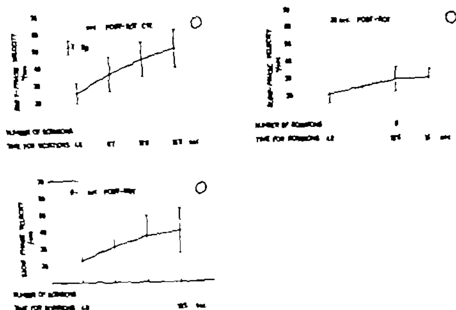


Fig. 3. Postrotatory slow phase ystagmus lecity f llowing increa ing mber of rot tions. ( ) A erage al es for the period 0–10 sec fter rot tion. (b) A erage lues for the period 10–20 sec fter rotation. ( ) A erag l es for the period 0–20 sec fter rotation.

in deg/sec for the following periods 0–10 sec, 10–20 sec and 0–20 sec where 0 indicates the point of complete stop of the chair

There w s no difference between reactions obtained early and late in the sessions and results for any specified number of rotations were lumped in the final calculations. There are considerable individual ariations as indicated by the S alues, but still they are within such limits as to form a reasonable ba is for comparison with other groups on a statistical basis. The best correlation between stimulus and response is obtained by measur ing in the period immediately after the rotation.

Bárány (1907) examined the postrotation responses in a large number of subjects. He measured the duration of nyst gmus when fixation of the eyes was inhibited by means of strong biconvex glasses. The response at tained a m ximum with 10 rotations during about 20 sec. This conclusion was based on the mean val es. Perusal of the a ailabl figures appear to indicate that persons with nystagmus of very long duration would have less reaction when the number of r tations wa increased. Persons with short lasting reactions, however apparently have a steadily increasing duration, when the period of rotation is extended. Our curves show a gradual decrease of response growth in tests with prolonged rotation. Possibly thi indicates n approach to a maximum of vestibular reactivity but it may also be an expression for some limit to the speed with which the eyes can perf rm nystagmus movements. Thus it is difficult to distinguish

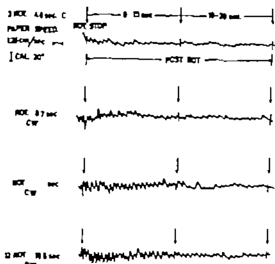


FIG. 2. Example of electronystagmographic response following increasing number of rotations.

The duration of each rotation period was measured by stop-watch. Variations for each set of tests were kept within one sec.

The subjects had closed eyes during the whole of each test run and were instructed carefully about the importance of keeping the eyes in a midline position during the recording. By observation of the closed eye-lid it was easy to certify that these instructions were followed.

Eye movements were recorded by electronystagmography (Fig 2) with electrodes taped by the outer canthi and an indifferent electrode on the forehead. The signal was amplified and transferred to the recorder by means of F.M. telemetry technique. The amplifier and F.M. transmitter together were of small dimensions and could be strapped to the chest without impeding free natural movements in any way. The use of this transmission technique reduced the time constant of recordings to almost one sec. Our equipment has been described in further detail by Osterhammel & Peitersen (1967).

RESULTS

All 9 subjects experienced considerable vertigo, when exposed to more than 3 rotations. Two became nauseated after the 9 and 12 rotation test, respectively, so that the session had to be discontinued. No one has suffered any lasting ill effects. For scoring of results it was evident that nystagmus duration would be of little value. Many subjects showed typical beats even after several minutes and the end point was not well defined. Furthermore there appeared to be no correlation between such long lasting reactions and the intensity of the early response.

The most consistent parameter was found to be the slow phase eye displacement immediately after the rotation. Fig. 3 shows slow phase velocity

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HISTOCHIMIE DE LA MUQUEUSE OLFACTIVE DE QUELQUES MAMMIFÈRES

P Ardouin C. David, et M Maillet
Tours France

Les pigment des muqueuses lfactives de ch iens, chats, chè es et vaches présentent d'intéressantes propriétés histochimiques communes à ces espèces, et appartiennent aux groupes des céroïdes, des mélanines et à certaines classes des chromolipoï les. Le chat c pendant, posséd quelques particularités, et des tra es d caroténoïdes ont été décelées au niveau des cellules épithéliales. Pa ailleu rs, une distinction est à établir entre les gra ulation pigmentaires des glandes de Bowman et les pigments de l épithélium.

La muqueuse olfactive des mammifères présente une certaine analogie structurale L épithélium comporte classiquement trois sortes de cellules

— cellules de soutien à noyau ovoïde

— cellules basales rangées en une seule assise

— cellules olfacto-sensorielles de Schultz, dont la morphologie est bien connue noyau très arrondi, cytoplasme bipolaire cils vibratils sur les vésicules olfactives.

Le chorion est criblé de glandes de Bowman dont la béance de la lumière varie suivant les espèces. Il est intéressant de noter que ces glandes sont absentes chez les animaux aquatiques et apparaissent pour la première fois dan la série des vertébrés, chez les batraciens

La grande particularité de la muqueuse olfactive est de contenir des granulations pigment ires jaunes ou brunes, visibles dans les glandes de Bowman, d ns les cellules basales et dans la région supra-nucléaire des cellules olfactives Leur rôle éventuel dans l olfaction n est pas clairement précisé t des informations sur leur nature et leurs propriétés sont rares bien qu des données intéressantes datent de 1922 (Parker) de précieux renseignements histochimiques sont fournis par Fortunato & Nicolini (1958) t ndis que l'Ecole belge avec *Gerebtzoff & Schkapenko (1952)* re lance ces études sur le plan biochimique

Les principaux résultats généralement admis peuvent être *résumés ainsi*

— il existe une relation étroite entre l'abondance des pigments et l'acuité de l ordorat chez les mammifères aériens.

— Les pigments sont d' rigine lipidique assez fortement insaturés

Tra il réalisé dans le cadre de la R. C. P pa le laboratoire d'Histologie de l Faculté de Médecine de Tours (Prof. *Maillet*) en collaboration avec la linique O. R L. du C. H U de Tours (Prof Ardouin) avec la participation technique de Mme D vid R.

between slow and fast phase during the early seconds of strong responses. As mentioned 4 subjects were submitted to 9 rotations in the counter clockwise direction at the end of the session The averaged results were as follows 0–10 sec 43 /sec 10–20 sec 29 /sec, 0–20 sec 36 /sec

These responses coincide very closely with the other results and support our impression that habituation did not occur to a measurable degree with the chosen procedure

ZUSAMMENFASSUNG

Neun Versuchspersonen wurden in einem manuell getriebenen Drehstuhl mit einer Schnelligkeit von ungefähr 280 /sek. in verschiedenen Zeiträumen rotiert. Beginn und Abschluss der Rotation war sehr plötzlich Das Ziel der Untersuchungen war ein Normalmaterial zu erhalten, womit wir eine Anzahl von *Ballettänzern vergleichen konnten um das Vorkommen von einer durch den* Ballettanz induzierten Habituation zu untersuchen Die Resultate wurden durch telemetrische Elektronystagmographie registriert Die Geschwindigkeit der langsamen Phase der Augenbewegungen in der ersten *postrotatorischen Zeit* wird zur Registrierung angewandt

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RÉSULTATS

1. *Fluorescence primaire*

Sur une coupe congelée de muqueuse olfactive des différentes espèces étudiées, certains pigments présentent une fluorescence primaire orangée et d'autre jaune-vert pour une excitation en U. V. intense. Pour cette même gamme de radiations, l'endothélium vasculaire apparaît en bleu clair.

2° *Dépigmentation*

	H_2O_2 à 3 vol. (24 h)		Chlore (2 h)		Eau de brome (1 h)		SO H (10 à 60 ., 10 à 24 h)		NaOH 2 (1 à 12 h)	
	E	G	E	G	E	G	E	G	E	G
Chien	+	+	− +	+	− +		+	+	+	+
Chat		− −	− −	+		+	+	+	+	+
Chèvre	+		+	+	− +	+	− +		+	+
Vache		±	+	+	+	+	+	+	+	+

E = Pigment de l'épithélium. G = Pigments des glandes de Bowman. + = Dépigmentation total + = Dépigmentation partielle ± = Dépigmentation douteuse

Ce tableau met en évidence une sensibilité lente des pigments vis à vis des acides et des bases.

Ceux du chien sont assez vite détruits par H_2O_2, alors que ceux de la vache, de la chèvre et surtout du chat offrent une résistance plus grande. Pour ce dernier animal, il faut une concentration en H_2O trois fois supérieure afin de réaliser une dépigmentation totale.

La dépigmentation par le brome est accélérée dans un solvant apolaire comme le CCl_4, tandis que ce dernier solvant dépourvu d'halogène ne provoque qu'un léger éclaircissement des granulations.

Le remplacement du brome par l'iode dans le tétrachlorure de carbone n'a aucune action. Il n'y a là aucune anomalie si l'on se souvient que l'iode est moins électronégatif que le brome.

3° *Solubilité*

Les granulations pigmentaires résistent au propylène glycol et aux solvants habituels des graisses, et le test à la fuchsine phéniquée confirme une alcoolo et une acido résistance.

Heusghem & Gerebtzoff (1953) par l'analyse biochimique, et prenant comme référence du caractère lipidique des substances, leur solubilité dans l'éther de pétrole, trouvent des composés pigmentés lipidiques et non lipidiques, et Philippot & Gerebtzoff (1956) aboutissent à l'hypothèse de l'hydrosolubilité des pigments et non à la liposolubilité comme on pourrait s'y

(Heusghem & Gereblzoff 1953 Philippot & Gereblzoff 1956 Gereblzoff & Schkapenko 1952 *Paulsen 1886) Ils appartiennent* au groupe des chromolipides

— La nature des sécrétions glandulaires est définie (Gereblzoff & Schkapenko *1952* Massei & Costa 1957 Jackson 1960)

— Des essais de recherches enzymologiques ont été abordés, particulièrement en ce qui concerne les phosphatases (Massei & Costa, 1957)

Cependant les questions suivantes restent posées

— S agit il pour l ensemble des pigments diversement localisés dans *la muqueuse d un animal déterminé d un même groupe de pigments*?

— Existe t il une identité de structure chimique entre les pigments des divers mammifères observés?

Pour préciser ces notions il apparait alors utile d apporter quelques informations complémentaires sur les propriétés physico-chimiques des pigments olfactifs, et plus spécialement chez le Chat le Chien la Chèvre et la Vache Tout d abord parce que les deux premiers sont des carnassiers réputés pour la finesse de leur sens olfactif et en ce qui concerne le Chèvre et la Vache, il semble utile de *prospecter des animaux dont* le sens de l olfaction est polarisé sur la recherche des aliments herbacés.

TECHNIQUES

Les fragments de muqueuse olfactive prélevés au plus tard vingt minutes après le sacrifice de l animal, suivent deux destinations

— certains sont fixés au formol à 10 % ou au bouin aqueux

— d autres sont congelés à 80 C dans un mélange acétone-neige carbonique

Les méthodes suivantes ont été appliquées à l étude de ce matériel

— *La dépigmentation est réalisée* soit par des halogènes (procédé de Mayer) soit par l acide per acétique selon la méthode de Lillie soit par H_2O_2, SO_4H_2, NaOH à des concentrations indiquées sur le tableau

La mise en évidence des *lipides est faite par les colorants habituels* des graisses, en particulier par le Noir Soudan B et par le Soudan III sur des coupes à congélation et sur des pièces fixées au formol calcium de Backer

La métachromasie est recherchée au moyen des Bleu de Nil Bleu de Méthylène et Bleu de Toluidine (pH 6)

L insaturation des lipides est vérifiée directement par O_4 Schiff et indirectement par le blocage des doubles liaisons, par halogénation et par oxydation au moyen de H_2O_2.

La réaction du P A S est réalisée par la méthode classique de Hotchkiss avec controle par acétylation

La détection des fonctions SH et SS est obtenue par le procédé de Chevremont et Frédéricq au cyanure et sulfate ferrique et par le procédé de Gomori au tétrazolium et au moyen du D D D

Le fer est révélé par la réaction de Perls

RESULTATS

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Le fer est révélé par la réaction de Perls



Fig. 2. Muqueuse olfacti d chien. Les pigments sont situés en dehors des ones présentant une positivité P A.S.

5° Caractères insaturés des pigments

Les pigments, les cellules glandulaires, les parties périphérique et super ficiell de l'épithélium, sont riches en composés insaturés. En effet

— Dans toutes les espèces, la coloration au sulfate d Bleu de Nil y est positive

— La réaction O_3-Schiff est positive également ce qui, selon Lison, témoigne en fa eur des phospholipides sensibles à l oxydation.

— Le caractère insaturé se retrouve dans le comportement des pigments is à vis de H_2O ou de H_2O Ces composés démasquent des fonctions carbonyles, puisqu après un tel traitement, l réaction du P A. S. augmente en intensité et en étendue et atteint les pigment ux mêmes.

Ce sont ces liaisons insaturées qui sont responsables d'une attaqu des halogènes (attaque additionnelle du type trans-) Un blocage des liaisons multiples par bromuration sur coupes congelées ou fixées, rend inefficace les réactions acide per-acétique-schiff



FIG. 1 Muqueuse olf cti de chèvre montrant l lco lo et l acido-résist nce à l ég rd de la fuchsine phéniquée

attendre cette hydrosolubilité serait empêchée par des liaisons avec des lécithines Une étude histo-enzymologique en cours nous permettra de revenir ultérieurement sur ce problème

4 *Complexe lipide pigment che. les quatre espèces étudiées*

Ce complexe présente un caractère basophile très prononcé dû à des groupements carboxiliques libres, et qui se manifeste par une métachromasie avec le Bleu de Méthylène le Bleu de Toluidine et le Bleu de Nil

	Bl de Nil 1,5	Bleu d Méthylèn 1,5	Ble de Toluidine 1,5
Chien			
Chat		Métachromasi des pigments du ch rion t de l épithélium	
Chèvre			
Vache			

Enfin, un blocage par acétylation empêche l'action du Schiff et les pigments des glandes prennent une teinte plus ou moins verdâtre.

— Par ailleurs, le Bleu d'alcian présente une similitude d'action avec le P. A. S. et les plages colorées dans les deux cas se superposent.

7. *Présence de soufre*

La fonction thiol et les ponts sulfhydriles ont été détectés au niveau des pigments, du cytoplasme des glandes et de l'épithélium. Sur les pièces congelées puis traitées par la méthode au ferricyanure et au sulfate ferrique les zones bleues correspondent à la fois à celles contenant des lipides, des mucopolysaccharides et des pigments.

Mêmes résultats avec la méthode utilisant le D. D. D. (disulfure de 2,2 dihydroxy-6-6'-dinaphtyl) copulant avec un sel de diazonium, en l'occurrence le Fast bleu B salt.

8° *Réaction de Perls*

Les résultats sont douteux dans l'ensemble des muqueuses olfactives. Les pigment ayant un fort pouvoir réducteur il est possible que le fer ferrique Fe^{+++} soit rapidement réduit en fer ferreux Fe^{++} et celui-ci capté sous forme de chélates, ou de complexes. D'où la difficulté de visualiser la réaction.

9° *Argentaffinité*

La très grande argentaffinité pigmentaire laisse penser qu'on est en présence de polyphénol et d'aldéhydes, c'est-à-dire de substances réductrices.

Avec le procédé Masson il n'y a pas que les pigments qui noircissent. D'autres granulati n relati ement abondantes et initialement incolores apparai sent. Il se pourrait que ces substances aient une fonction aldéhydiqu libre.

10 *Reactions d caroten ïdes*

Un solution iodo-iodurée ne f rme aucun dérivé iodé avec les pigments des chiens, chèvres et vaches. Les caroténoïdes sont d nc absents de la muqu use.

La seul exception rencontrée est celle des pigments de l'épithélium du hat : ceux-ci ont donné un test soit douteux, soit légèrement positif.

Il est intéressant de noter que Goodwin (1952) avait déjà décelé chez le chat des traces de ces pigments dans l'épithélium de la muqueuse olfactive alors que chez les autres vertébrés, ces pigments ne se retrouvent pas. Quand on se souvient que les caroténoïdes sont des pigments photosensibles qui interviennent dans l mécanisme de la vision, on ne manque pas d'y apporter une certaine importance à ce problème.



Fig. 3 Pigment de la muqueuse olfactive de chat sur coupes congelées.

6 *Absence de groupes polysaccharidiques dans la structure pigmentaire*

— *Une digestion amylasique durant 5 heures laisse les pigments intacts* alors que le reste de la cellule qui les contient est plus ou moins digéré.

— La réaction du P A S est nettement positive au pôle interne et sur les plages latérales des glandes.

Par contre au niveau des pigments, elle est négative chez les quatre espèces étudiées (l'hydrolyse par l'acide per iodique n'étant pas prolongée au delà de 15 mn.)

Chez la vache on peut remarquer que toute la surface de l'épithélium n'est pas uniformément rose seules la vésicule olfactive et les régions périphériques sont positives. Chez le chien les glandes de Bowman et les cellules basales rejettent vers l'extérieur de la muqueuse des granulations P A S positives, *mais celles-ci par leur morphologie et leurs propriétés* ne sont pas de même nature que les pigments classiquement définis. Ces résultats se retrouvent tant sur les coupes congelées que sur les coupes fixées.

Propriétés communes aux quatre espèces

— Destruction facile par les oxydants puissants
— Nature lipoïdique et fortement insaturée
— Ce sont des composés soufrés ne présentant pas de sensibilité au P A S. et au Bleu d'alcian contrairement aux sécrétions des glandes de Bowman et des cellules épithéliales
— Ils appartiennent tous aux groupes des céroïdes, des mélanines, et à certaines classes de chromolipoïdes, et ne sont jamais excrétés.

Propriétés particulières au Chat

— Plus grande résistance vis à vis des oxydants comme H_2O_2.
— Sensibilité moins nette aux colorants des graisses.
— Présence de groupements aldéhydiques libres dans certaines granulations pigmentaires.
— Présence pos ible de caroténoïdes au niveau des cellules épithéliales.
— Aspect général des pigments et leur nombre très différents des granulation des autres espèces.

	Dimensions des pigment en μ	Leur aspect	Les nombre dans 1 cellule
Chat	0,6 à 3,75	Plaquettes	3 à 10
Chien	0,33	Sphérules	Ind. terminable
Chèvre	0,20	Sphérules	Ind. terminable
Vache	0,20	Sphérules	Indéterminable mais souvent une inégalité

Enfin dan une même expèce animal il ressort de l étude des tableaux qu une distinction doit être faite entre les pigments de l'épithélium et ceux des glandes leurs réponses aux réactions histochimiques ne sont pas toujours identiques. Les pigments situés dan les glandes ne sont jamais expulsés et sont de taille plus importante que ceux localisés dans les élé ment nerveux de l'épithélium

Cette discrimination pourrait remettre ainsi en question la définition même du pigment olfactif Peut-on dire que toutes les granulations pigmentaires d la muqueuse olfactive soient des pigments olfactifs Ou peut-on considérer qu les seul pigments dits olfactifs soient ceux du yt plasme de la cellule neurosensorielle, et réserver le terme plus général d granulati ns pigmentaires au reste des pigments de la muqueuse Car dire qu un pigment est olfactif c est laisser supposer son rôle dan l olfaction Or la nature même des pigments étudiés ne permet pas de leur attribuer un r l physiologique si important. Il est probable qu'ils ne soient que les résultats d'un schunt secondaire dans les métabolismes lipidiques et protéidique

	P A S		P. A. S bloqué par acétylation		H_2O_2 à 1 vol. 36 h, puis P.A.S		Bleu d'Alcian		Fuchsine phéniquée		Argent affinité		Réaction de Perls	
	E	G	E	G	E	G	E	G	E	G	E	G	E	G
Chien	CB + SE + P –	GB + + +	–	–	CB + SE + P ±	GB + + + I ±	CB + SE + P –	GB + P –	+	+ +	+	+	–	
Chat	CB + SE + P –	GB + + I ±	–	–	GB + + + P ±	GB + + + P ±	GB + SE + P –	CB + + P ±	+ +	+	+		+	
Chèvre	CB + SE + P –	CB + + I –	–	–	GB + + + P	GB + + + P –	CB + SE + P –	GB + + P –	+	+	±	+		
Vache	CB + SE + + P –	GB + + P ±		–	CB + + + P	CB + + + I ±	CB + SE + + I –	GB + + P ±	+	+	+	+		

CB = Cellules basales. SE = Surface épithéliale. GB = Glandes de Bowman. P = Pigment. E = Epithélium. G = Glandes.
+ = Réaction positive. + + = Intensité croissante. + + + = Avec le nombre de +. – = Réaction négative. ± = Réaction douteuse.

11° *Réactions des céroïdes*

La présence des céroïdes est probable car la résistance à l'acide et à l'alcool dans l'action de la fuchsine phéniquée en est une caractéristique.

12° *Réactions des mélanines*

L'examen des propriétés (affinités tinctoriales, réaction des lipides, solubilité et fluorescence) ainsi que la réduction du nitrate d'argent ammoniacal permettent d'identifier des mélanines.

13° *Réactions des chromolipoïdes*

La réaction de Hueck laisse un certain nombre de grains bleus de chromolipoïdes, mais la réaction de Mallory n'indique pas d'hémofuscine et le test de Schmorl ne penche pas en faveur des lipofuscines.

CONCLUSIONS

L'étude histochimique comparative de la muqueuse olfactive du Chat, du Chien, de la Chèvre et de la Vache, montre en ce qui concerne les pigments des propriétés communes et des propriétés toutes particulières au Chat.

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AIRWAY OBSTRUCTIONS IN LARYNGECTOMIZED PATIENTS

A Spirometric Investigation

W. TORNLAMS

From the Department of Otolaryngology and the University Institute for Respiratory Physiology, Ullevål Hospital, Oslo, Norway

It is obvion that the mecha ics of breathing will be involved in la ryngectomized patients. Probably the changes in the respiratory tract fter laryngectomy will le d to reduced pulmonary ventilation. The ventilatory capacity in 14 lary gectomized patient has been measured by mea s of dynamic spirometry using the vital capacity (VC), forced expiratory volume in on second (FEV) and the maximal voluntary ventilation (MVV) as parameters. Spirometric in estigation has also been performed in a healthy female and the measurements were repeated fter breathing through an artificial stenosis of different degrees to demonstrate the change of the spirometric pattern following stenosis of the trachea. All the patients showed red ced pulmonary ventilation caused by airway obstructions, and the spirometric patterns were mostly in ccordan e with stenosis of the tra hea. It was demonstrated that good correlation exist between the impairment of the pulmonary entilation and the tenden y f shrinking tracheostoma

One of the most important physiological alterations which takes place in patients after laryngectomy is the change in *respiratory function*. Because of the shortening of the conducting airway with breathing through a tracheostoma the inspired air is neither saturated with water vapour nor warmed to body t mperature before it reaches the lower respiratory tract. The result will be reduced ciliary activity (Toremalm, 1961) and damaged epithelium of the respiratory mucous membrane which leads to metaplasia of the normal ciliary epithelium (Friedberg *et al.* 1964). Jackson & Jack son (1950) emphasize the importance of (1) ciliary activity (2) tussive sqeeze and (3) bechic blast for normal pulmonary drainage and conclude that anything that lessens these physiologic mechanisms promotes bronchial obstruction. A clear airway is f decisive importance in maintaining normal pulmonary ventilation. A normal function of the larynx is greatly involved in the ventilatory mechanism: (1) In maintaining a free airway by removing mucous and particles which may obstruct the respiratory tract during cough. (2) The dynamic of the larynx regulates and distributes the

SUMMARY

The pigmentation of the olfactory mucosa of dogs, cats, goats and cows presents some interesting common histo-chemical properties belonging to the ceroide, melanine and certain chromolipoid groups. The cat however possesses several *histo-chemical particularities*, plus some carotenoidal pigmentation which has been revealed on the epithelial cellular level. On the other hand a distinction has been made between *the pigmentary granulations of Bowman's glands* and the epithelial pigmentations.

ZUSAMMENFASSUNG

Die Pigmentierung der olfaktiven Schleimhaut der Hunde Katzen Ziegen und Kühe zeigt gemeinsame histochemische Merkmale hinsichtlich der Gruppe der Steroiden Melaninen und einiger Chromolipoiden Die Katze besitzt mehrere histochemische Eigentümlichkeiten und einige karotinoide Pigmentierungen die man in dem Epithel der Schleimhaut findet Andererseits hat man einen Unterschied zwischen den körnchenbildenden Pigmentierungen der Bowmanschen Drüsen und denen des Epithels feststellen können

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W. TORJUSSEN

From the Department of Otolaryngology and the University Institute for Respiratory Physiology Ullevål Hospital Oslo, Norway

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SUMMARY

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Fig. 1. Spirometric investigation of laryngectomized patient coupled to the spirometer by means of rubber mouthpiece fastened with adhesive plaster and neck strap.

None of the patients had ever suffered from pulmonary diseases, except one patient who had pleurisy many years ago. One patient was digitalized and one had a heart infarction some years ago. Twelve patients were smokers and eleven heavy smokers during more than twenty years. Two patients had never smoked at all (numbers 3 and 12, Table 1).

RESULTS

Table 1 shows the results of our measurements and the mean figures of the three parameters: vital capacity (VC), maximal voluntary ventilation (MVV) and forced expiratory volume in one second (FEV_1).

VC and MVV are transformed into percentage of standard references worked out by Storstein & Voll (1962). FEV_1 is, on the other hand, expressed in per cent of VC (FEV_1 %).

The mean figure of VC% of about 100 suggests that there are no restrictive pulmonary changes of importance in our material. A range varying

air flow to the alveoli of the lungs. Ogura *et al* (1966) have recently established that airway resistance due to nasal obstruction influences the pulmonary mechanics of breathing apparently through a reflex arc. It is likely that similar reflex connections may exist between the larynx and the pulmonary function

As already pointed out by Heyden (1950) it is probable that the changes in the respiratory tract after laryngectomy will lead to reduced ventilatory pulmonary capacity by obstruction of the conducting airway At Ullevål Hospital Oslo we have got the impression that dyspnea after small exertions is a frequent complaint in laryngectomized patients Some of these patients have connected this complaint with narrowness of tracheostoma.

The purpose of this investigation has been to measure the pulmonary ventilation in patients after laryngectomy by means of spirometry in order to find out whether the ventilation might be reduced to such a degree that the working capacity of these patients is seriously impaired

METHODS

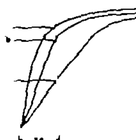
To judge the ventilatory ability of the lungs a spirometer constructed at the University Institute for Respiratory Physiology Oslo, has been used The resistance of the spirometer to breathing is minimal The paper barrel has variable speed (120 mm/min 600 mm/min and 1200 mm/min) which is necessary when performing dynamic spirometry

All the measurements of the pulmonary function quantities used in this investigation are corrected to 37 C, saturated with water vapour and registrated at ambient pressure (BTPS) Spirometric registrations of vital capacity (VC) forced expiratory volume in one second ($FEV_{1.0}$) and maximal voluntary ventilation (MVV) have been performed with the patients in sitting position The patients were coupled to the spirometer by means of a common rubber mouthpiece which was connected closely to the tracheostoma with adhesive plaster and fastened with a neck strap (Fig 1)

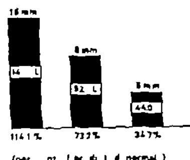
The measurements of each parameter were repeated three times, and the most successful reading was employed With regard to the terminology for the spirometric measurements used in this investigation, we have employed the terms recommended by Comroe *et al* (1962)

MATERIAL

During the period from January 1960 to March 1965 23 patients have been operated for carcinoma of the larynx at Ullevål Hospital (Ear Nose and Throat Department) Eighteen patients were treated by total laryngectomy but 3 patients had died before the investigation was started in the first half of 1965 One patient did not cooperate in the investigation so the material consists of *14 laryngectomized patients* (Table 1)



F g. 2.



F 3.

Fig. 2. Three different spirometric registrations of the forced expiratory olume in one second (FEV 1.0) i f male, 21 years old, with healthy l ngs (vital capacity: 4317 ml) FEV is regi trated under normal condition with free airway ( ) nd with different degrees of stenosis, (b) nd ( ) After maximal in piratio the trial person is ked t expire with ma imal effort, nd the l olum expired in one second is meas red From the formula FEV 1.0/VC 100 the FEV% I calculated (see text) a, Free airway diameter 16 mm, FEV% 86.8 FEV 1.0 3740 ml; b stenosis, diameter 8 mm, FEV%: 76.5, FEV 1.0 3272 ml stenosis, diameter 5 mm, FEV% 42.0 FEV 1.0 1813 ml.

Fig. 3 Diagram demonstrating three different mea urements of the maximal vol ntary entilation (MVV) in 21 years-old female with healthy lungs. MVV is measured nder normal conditions with free airw y (diameter 16 mm) d with different degrees of stenosis (8 mm and 5 mm) The measurement of the MVV re transformed int per cent of predicted normals using the formul worked out by Storstei & V ll (1952)

ery little influence upon the am unt of air that it is possibl to inspire or expire, but it may affect the time required to do a maximal inspiration or expiration Therefore the vital capacity most often shows normal values (Carlens, 1954) Reduction of the dynamic spirometric quantities and normal static spirometry expressed by VC is also the typical pattern of this trial.

Under normal conditions the glottis is the narrowest part of the upper conductive airways, or it may be regarded as the physiological stenosis of the trachea (transformed into a circular cross sectional area with a diameter of 16 mm, i.e. in section 2 cm²) In this investigation spirometry ha lso been carried out in a healthy female with free airways. The dynamic spirometri parameters have also been registrated after applying artificial, circular con trictions with diameters of 8 mm and 5 mm (cor responding to an ordinary tracheal cannula and a severe tracheal stenosis) The constriction were made by boring circular holes in a thin plastic pl t Thi sort of perforated membrane was placed in the tube between th mouthpiece and the spirometer The same diameters have been used by Ingelstedt & Toremalm (1961) in their tracheal model constructed for investigations of air flow and heat transfer within the airways

TABLE 1 *Values (BTPS) of spirometric ventilatory measurements in 14 laryngectomized patients*

Patients (No. init. sex)	Age (yrs)	Height (cm)	VC (ml)	MVV (l/min)	FEV (ml/sec)	% of predicted normals VC%	MVV%	$\frac{FEV_{1.0} \times 100}{VC}$ (FEV %)	MVV/VC (l/ml)
1 O W o	68	180	3190	71.2	2310	6.4	59 7	72.4	[illegible]
2. R. B o	56	171	5049	112.6	2904	125.2	80 7	57.5	0.44
3 A L. ♀	72	160	2310	83.1	1787	90 0	91 8	77 4	1.0[illegible]
4 J E. o	70	180	3795	77 4	2612	92.3	67.2	68.8	0.7
5. A. A. o	65	174	3712	96.3	2761	94.8	78.6	74.3	[illegible]
6. R. G ♂	64	175	2673	32.5	1826	66.7	26.0	68.3	0.39
7 K F o	60	171	3822	110 0	2585	98 0	83 7	67 6	[illegible]
8 G S. o	55	1 6	4427	60.2	2134	101 4	41.8	48.2	0.41
9 R O o	58	172	4152	77 0	2090	103.2	56.7	50.3	0.55
10 H. N ♂	59	169	4103	93.2	2783	107 7	70.3	67.8	0.65
11 G A. o	74	166	3217	44 0	1424	102.7	43.6	44.2	[illegible]
12. B B	51	172	5621	142 1	4433	132.0	94.7	78.8	0.71
13. E. S. o	56	178	4400	82.9	1892	93 8	44.1	43.0	0.41
14 N N o	53	180	5538	110.6	4213	118.5	79 9	76.0	0.87
Mean	61.5	173 1	4000 6	84 4	2553.8	100.5	65.6	63.9	0.65

The mean difference, VC% – MVV% is statistically highly significant ($t = 7.12$) (A. B. Hill *Principles of Medical Statistics* p. 149) To calculate the predicted normals the formulae worked out by Storstein & Voll (1962) are used

from 66 7% to 132 0% implies that there is no greater variation than might be found among persons with healthy lungs.

The mean MVV% is, on the other hand surely reduced compared to the mean VC% and this reduction is statistically highly significant ($t =$ 7 12) calculated by means of the *t test* (A B Hill 1961 p 146)

FEV % is also reduced to a mean of 63 9% In control materials of normal persons FEV % lies between 80 and 85% (Comroe *et al* 1962, p 200 Engstrom *et al* 1964)

DISCUSSION

It is permissible to conclude that in this investigation of 14 laryngectomized patients a significant degree of airway obstruction has been found Whether the reduced ventilatory capacity is due to widespread obstructive changes of the tracheo-bronchial tree or caused by a more localized stenosis of the trachea is so far difficult to decide If the latter explanation is right it is probable that postoperative alterations in or near the tracheostoma have been the cause of the obstruction A moderate stenosis in the airways has

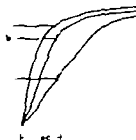


Fig. 2.

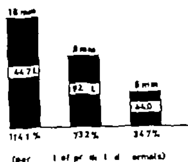


Fig. 3

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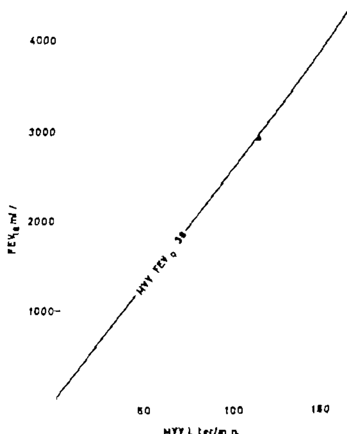


Fig 4 The rel tionship between the spirometric regi tratio s f FEV and the MVV in 14 laryngectomized patient (see text)

Figs 2 and 3 illustrate that both the parameters $FEV_{1.0}$ and MVV are distinctly diminished when the cross sectional area is reduced from the physiological stenosis of a normal adult larynx of 2 cm² to 0.5 cm² when the diameter is halved from 16 mm to 8 mm This will reduce the FEV % from the normal 86 6 to 75.8% (Fig 2) and MVV from 144 7 l/min to 92 8 l/min (Fig 3) Further reduction of the stenosis to 0.2 cm² will lead to a great reduction of FEV % from 75 8 to 42 0% and MVV from 92 8 l/min to 44 0 l/min, even though the diameter will be reduced by only 3 mm These findings will explain why small children with a narrow airway may develop great respiratory difficulties caused by a slight swelling of the respiratory mucous membrane

It has been maintained (Bass, 1959 Kennedy 1953) that MVV in patients with obstructive pulmonary diseases could be determined indirectly by multiplying $FEV_{1.0}$ by a factor ($MVV = FEV_{1.0} \times 38$) This is correct only if there is no airway obstruction or when we have to deal with reduced pulmonary ventilation on account of mainly impaired expiration (e.g bronchitis, asthma, emphysema) This correlation does not exist in our trial with artificial stenosis or in our material of laryngectomized patients (Fig 4)

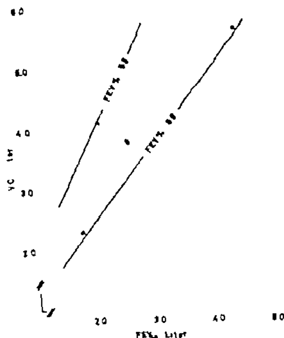


Fig. 5. The relationship between the spirometric registrations of the FEV and the VC in 14 laryngectomized patients (see text)

Fig. 4 demonstrates the relationship between the two parameters FEV$_1$ and MVV in this material MVV is more often reduced than FEV . This indicates indirectly that the airway obstructions found in the patients after laryngectomy affects both the expiratory and inspiratory phase of the breathing. These findings are in agreement with Engström *et al* (1964) who performed dynamic spirometry in 41 patients with localized stenosis of larynx and trachea and pointed out a marked discrepancy between FEV and MVV These authors also found that partial release of the obstruction by tracheotomy in one half of the cases resulted in a more pronounced increase in MVV than might be expected from the change of FEV du to the stenotic affection of both the expiratory and inspiratory phase of breathing The investigation of Schiratzki (1965) also suggests that in patients with upper airway obstructions due to paralysis of the recurrent laryngeal nerve, the MVV is more often reduced and to a higher degree than the FEV .

Fig. 5 shows that in all the 14 patients in this investigation a lowered FEV % is observed The single measurements however demonstrate that even moderat lowered FEV% may lead to *considerable reduction of the* ventilatory capacity expressed by the parameter MVV because *the air resistance* f the inspiratory phase of breathing could be more pronounced than

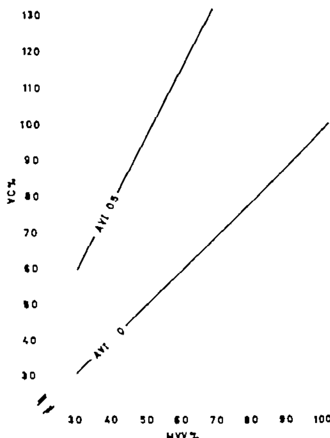


Fig 6 The relationship between the MVV % and the VC% of predicted normals in 14 laryngectomized patients This relationship is called the air velocity index (AVI) (see text)

the air resistance of the expiratory phase (Table 1) Hence it seems to be obvious that MVV which takes into account both the phases of breathing has been the best parameter in judging the degree of airway obstruction in this investigation

By calculating the ratio between MVV and VC expressed in per cent of predicted normals, an expression of the air velocity index (AVI) is made (Fig 6) An index lesser than 1 0 suggests an obstructive airway disease but a low value is not diagnostic of any single disease or disorder (Comroe *et al* 1962 p 203) MVV % lesser than 60 % is found in 0 of the 14 patients. Measured in liter per minute the MVV in this group are in the range of 32 to 71 l/min These figures, however are expressing the maximal ventilation the patients can maintain during a very short period If the normal resting ventilation in healthy adults is calculated in the interval of 7–11 l/min and the need of ventilation by slow walking on a flat floor of 12–19 l/min the real meaning of the reduced MVV measurements found in this investigation can easier be understood

The airway obstructions shown in the spirometric investigation have hitherto been suggestive of stenosis of the trachea This suggestion can be

TABLE 2 *The material divided in groups on the basis of the MVV %*

	No. of patient	Wearers of cannula
Group		
I (MVV < 60%)	6	5
II (MVV 60–80%)	4	1
III (MVV > 80%)	4	0
Total	14	6

drawn on account of the spirometric pattern which shows an obvious reduction of both the inspiratory and expiratory air flow rate combinated with lack of reduction of the static lung volume VC. It is reasonable to suppose that constrictions in the tracheostoma or its surroundings are the reason why the reduced ventilatory ability has been measured in these patients.

In Table 2 the material is divided in three groups on the basis of the MVV-measurements. In group I there was a tendency in all the patients to have shrinking of their tracheostoma. Five of the patients in this group had been wearers of cannula and the sixth had been reoperated on account of shrinking of the stoma. In the second group one patient was wearing a cannula two hours a day because of a narrow tracheostoma. This patient also showed the lowest MVV measurement in group II. The remaining patients in groups II and III had no problems concerning their tracheostoma.

A simple complement to Table 2 might be to measure the cross-sectional area of the external opening of the tracheostoma. On account of the irregular form of the external opening this has been difficult to perform. Measurement of the external opening of the tracheostoma is probably of less importance in judging the degree of the stenosis, because X-ray studies with tomography has proved that the narrowest part of the stoma may as well be found inside the external opening of the tracheostoma.

CONCLUSION

Spirometric measurement in 14 laryngectomized patients indicates airway obstruction of different degrees in all the patients. The pattern of the spirometric parameters used in this investigation is most clearly in accordance with stenosis of the trachea. Obviously there is a good correlation between the tendency of a shrinking tracheostoma and impaired pulmonary ventilation, which in half of the patients is so far reduced that one is allowed to suppose serious involvement of working capacity.

ZUSAMMENFASSUNG

Es ist einleuchtend dass die atmungsfunktionelle Mechanik bei laryngektomierten Patienten wesentlich geändert wird Wahrscheinlich werden diese Änderungen zu einer herabgesetzten Lungenventilation führen Bei der vorliegenden Untersuchung wurde bei 14 laryngektomierten Patienten die Lungenventilation mittels dynamischer Spirometrie gemessen wobei die Vitalkapazität (VC) die maximale voluntäre Ventilation (MVV) und gesteigertes expiratorisches Volumen (FEV) as Parameter Verwendung fanden Die gleichen Parameter wurden bei einer gesunden Frau wo die Messungen nachdem unterschiedliche künstliche Stenosen in das spirometrische System wiederholt eingeschaltet waren, vorgenommen wurden Dies wurde getan um die Änderungen die bei diesen Parametern im Falle einer Trachealstenose vorliegen festzustellen Sämtliche Patienten im Untersuchungsgut zeigten eine herabgesetzte Lungenventilation wegen Verjüngung der Atmungswege Die Erfolge der spirometrischen Messungen zeigten gute Übereinstimmung mit denen der Trachealstenose Gute Übereinstimmung zwischen schlechter Lungenventilation beurteilt durch MVV Messungen und Schrumpfung der Trachea wurden festgestellt

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FUNKTIONELLE UNTERSUCHUNGEN DER PHARYNGO-OESOPHAGUS-STIMME NACH LARYNGEKTOMIE

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Es wird über phoniatrische und röntgenkinematographische Untersuchungen bei 25 Patienten berichtet und deren Ersatzsprache nach Laryngektomie geprüft. Es konnte gezeigt werden, dass die Form der Pseudoglottis und die Funktion der Ersatzsprache am besten röntgenkinematographisch zu analysieren ist. Dabei sind durch Untersuchung des Patienten mit Phonation nicht nur im Stehen, sondern auch im Liegen zusätzliche Informationen zu gewinnen, die die weitere phoniatrische Behandlung unterstützen. Die Ergebnisse sollten an einem grösseren Krankengut überprüft werden.

Trotz der kurativen Erfolge der operativen Kehlkopf-karzinom-Behandlung bleibt noch immer das Problem der Ersatzsprache. 100 Jahre nach den ersten Bemühungen um einen künstlichen Kehlkopf (Billroth 1872, 1874) haben viele Patienten nach Laryngektomie keine Ersatzsprache und versuchen, das Sprachproblem mit Hilfe von Sprechgeräten zu bewältigen. Für diese Patienten ist es zumeist schwierig, im Berufsleben wieder Fuss zu fassen.

Mit dem Problem der Ersatzsprache — der Pharyngo-Oesophagusstimme — beschäftigen sich eine Vielzahl von Publikationen. Seeman hat 1924 die Physiologie der von ihm als „Oesophagusstimme" (1920) bezeichneten Ersatzsprache beschrieben. In den letzten Jahren wurde neben dem Oesophagus und der für die Sprachbildung notwendigen Aerophagie der sog. „Pseudoglottis" eine grössere Bedeutung zugesprochen. Dabei soll die Güte der Ersatzsprache zu einem nicht geringen Teil von der Form und Lokalisation der Pseudoglottis abhängen (Luchsinger 1952, di Carlo et al. 1955, Möckel & Schlosshauer 1955, Damste 1957, Pommez & Landeau, 1961, Fumeaux, 1961, Cernoch & Zobril 1961, Dey & Kirchner 1961, Levin, 1961 u. a.).

Auf die besondere Bedeutung der Luftfüllung der Speiseröhre und die für die Güte der Sprache wichtige Form und Grösse des Windkessels hat Beckmann (1954) nach gemeinsamen Untersuchungen mit Diethelm hingewiesen. Während der praephonetischen Phase gibt es drei verschiedene Möglichkeiten der Luftaufnahme in die Speiseröhre. Sie sind charakterisiert durch die Begriffe

1 Inhalation
2 Aerophagie
3 Injektion

Unter Injektion versteht man in diesem Zusammenhang die zur Lautbildung erlernbare artikulatorische Einstellung der Zunge Die phoniatrische Unterweisung und Übung mit dem Patienten ist dabei die Grundlage für eine vom Patienten selbst fortzusetzende Sprachschulung (Moolenaar Bijl et al 1956 Seeman 1958 Moses, 1958 Levin S K u a)

Unabhängig vom postoperativen Verlauf wird auch der Einfluss der Operationstechnik auf die Ersatzsprache diskutiert Während Robe et al. (1956) den Standpunkt vertreten dass die Operationsart keinen Einfluss auf die Ersatzsprache hat sind andere Autoren der Meinung dass der Erwerb einer Ersatzsprache und deren Qualität vom operativen Trauma abhängen (Hodson & Oswald 1958 Sercer 1959 Taptapova 1960 Vallancien & Dinville 1962)

Neben diesen durch Morphologie und Funktion bedingten Einflüssen auf die Ersatzsprache wird auch die Rolle psychischer Faktoren diskutiert (Filkin 1953 McCall 1955 Stoll 1958) Es ist noch nicht geklärt welcher dieser drei Faktoren ausschlaggebend ist oder ob ihre Bedeutung im Individualfall nicht doch unterschiedlich ist

Eigene Erfahrungen in der phoniatrischen Praxis zeigten (Mitrović) dass erhebliche Unterschiede bei der Ersatzsprache bestehen die sich dadurch charakterisieren lassen dass manche Patienten die Sprachbildung unabhängig von der Korperlage muhelos ausführen konnen und andere in bestimmten Körperlagen (z. B Seitenlage) eine in anderer Lage noch vorhandene Stimme nicht produzieren können Aus dieser Beobachtung ergab sich die für die vorliegende Mitteilung zugrunde liegende Untersuchungstechnik

Wir stellten uns folgende Fragen

1 Kann man in verschiedenen Lagen bei der röntgenologischen Analyse der Ersatzsprache zu einer besseren Beurteilung über den Sitz und die Form der Pseudoglottis gelangen
2 Zeigen die für die Sprachbildung wichtigen Luftraume in unterschiedlicher Lage einen veränderten Befund?
3 Ist ein Unterschied in der Form der Pseudoglottis in Abhängigkeit zum vorausgegangenen Operationstermin und der Güte der Pharyngo-oesophagusstimme erkennbar
4 Kann die regelmässige Rontgenkontrolle der Sprachbildung dem Phoniater bei der Rehabilitation Laryngektomierter helfen?

KRANKENGUT UND TECHNIK

Bei 25 Patienten wurde eine gleichartige phoniatrische und rontgenkinematographische Untersuchung ausgeführt Vorausgegangen war bei den

Tabelle 1

	Jahre				
Altersgruppe	41–50	51–60	61–70	über 71	Anzahl
Patienten	2	8	11	4	25

Tabelle 2

Gruppe	I	II	III	IV	Anzahl
Zeitpunkt nach der Operation	bis zu 3 Monaten	bis zu 1 Jahr	nach 1 Jahr		
	erst. Versuche mit Oes. Stimme	Flüstersprache und 1–2 silbige Wörter	flüssige Ersatzsprache	Sprecher I	
Patienten	6	13	3	3	25

Patienten eine Totalexstirpation des Kehlkopfes nach BETHI mit einseitiger Neck Dissektion. 24 Patienten waren 1965–1967 operiert worden und ein Patient hatte die 5jährige Überlebenszeit bereits überschritten, ohne dass eine Halslymphknotenausräumung vorgenommen worden war. Im Rahmen der postoperativen Betreuung hatten diese Patienten eine phoniatrische Übungsbehandlung (Abteilung für Hör-, Stimm- und Sprachstörungen der Hals-Nasen-Ohren-Klinik Mainz. Leiter: Prof. Dr. P. Biesalski) erfahren. Ihre Altersverteilung geht aus Tabelle 1 hervor. Die Güte der erlernten Ersatzsprache bei den Patienten war sehr unterschiedlich und in 4 Gruppen einteilbar (Tabelle 2).

Die röntgenologische Analyse der Ersatzsprache erfolgte in der Weise, dass die Patienten im Anschluss an eine Kontrastmittelpassage mit Darstellung des Hypopharynx und Oesophagus aufgefordert wurden, die Vokale a, e und i zu sprechen. Zusätzlich wurde der Vorgang der Sprachbildung beim Sprechen eines Satzes oder mehrsilbigen Wortes geprüft. Es wurde versucht, den gleichen Untersuchungsgang (Breischluck, a-, e-, i-Phonation) nicht nur bei aufrechtstehenden Patienten, sondern auch in Rückenlage, Trendelenburglage, linker Seiten- und Bauchlage zu dokumentieren. Bei 2 Patienten war dies nicht möglich und die Untersuchung erfolgte nur in 3 Positionen. Dieser Modus der Untersuchungstechnik war für die Patienten nicht ohne Anstrengung, da neben der röntgenkinematographischen Dokumentation auch jede Phase der Phonation in jeder Position auf Röntgenzielaufnahmen festgehalten wurde. Grundlage für die Beantwortung der eingangs gestellten Fragen war die Analyse der Röntgenaufnahmen und -kinematogramme sowie der Versuch der Korrelation von Röntgenbefund mit der auf Tonband aufgenommenen Ersatzsprache.

ERGEBNISSE

1 Analyse und Beurteilung der Form der Pseudoglottis ist bei Patienten, die eine gute Ersatzsprache haben und deren Operation längere Zeit zurückliegt schon in aufrechter Haltung gut möglich Bei frisch Operierten war dagegen der Nachweis der Pseudoglottis im Stehen erschwert oder nicht möglich Die Untersuchung in Rücken und Bauchlage zeigte uns auch in diesen Fallen eine anatomische Einschnürung im Bereich des Oesophagusmundes Es dürfte sich dabei um den erhaltenen Anteil des M cricopharyngicus handeln der sich bei weiterer Sprachbildung zur Pseudoglottis entwickelt Die Analyse in verschiedener Korperlage zeigte weiterhin dass sich die Pseudoglottis nicht zu jedem Zeitpunkt bei dem gleichen Patienten an der gleichen Stelle bezogen auf die Halswirbelsaule befindet Vielmehr kann sie mit dem Schluckakt der Korperlage und der Phonation eine Verlagerung in craniocaudaler Richtung erfahren Durch narbige Fixation kann diese Beweglichkeit vermindert sein oder zusätzlich eine Lateralbewegung erfahren Für eine topische Angabe über die Hohenlage der Pseudoglottis eignet sich allein die seitliche Projektion da nur hier die unterschiedlichen Formen der Wirbelsaulenhaltung als Storfaktor auszuschliessen sind Die Höhenlage der Pseudoglottis variiert bei dieser Betrachtung zwischen dem 5 und 7 Halswirbel

2 Über die Bedeutung der Luftfüllung von Oesophagus und Hypopharynx in Abhängigkeit von der Korperhaltung können wir noch keine endgültigen Aussagen treffen Es war jedoch festzustellen dass Patienten mit einer schlechten Ersatzsprache die im Stehen entweder keine Luft bis in die Speiserohre bringen konnten oder aber zuviel Luft in der Speiseröhre aufwiesen im Liegen eher die Luft konzentriert ausgestossn haben Dies war erkennbar an der Tatsache dass im Stehen die Speiseröhre wahrend der Phonation entweder in ihrer ganzen Länge luftgefullt oder vollig kontrahiert und ohne Luft war wahrend sie sich im Liegen in den caudalen Abschnitten kontrahiert zeigte und die Luft den oberen Oesophagus ballonformig erweiterte Die geringere Kraft die der Patient im Liegen benötigt und die verstärkte Bauchpresse dürften hierbei unterstützend wirken

Die Untersuchung in Seitenlage schliesslich zeigte die dorsale Lokalisation der Pseudoglottis ihre Grösse und Hypertrophie sowie die Luftfüllung des Hypopharynx, dessen Beurteilbarkeit bei sagittaler Projektion durch Überlagerung mit Unterkiefer und Halswirbelsaule deutlich eingeschränkt ist

3 Die Form der Pseudoglottis lässt sich schwer quantitativ in Zahlen angeben Zwei Grössen waren jedoch gut erkennbar die Länge des bei der Phonation kontrahierten Abschnittes im operativ geschaffenen Übergangsgebiet von Hypopharynx und Oesophagus, und die Weite des Ansatzstückes im Bereich der Pseudoglottis für den Luftdurchtritt Bei einer guten Ersatzsprache fanden wir eine scharf konturierte nur etwa 1/2 bis 1 cm in



Abb. 1 Lary gektomierter P tient der I. Gruppe. Röntgenaufnahmen des Hypopharynx od Oesophagus während) des Schluckaktes mit Bariumbrei, b) A-Phonation in Rückenlage,) E-Phonation i Bauchl ge Die Pseudoglottis erstreckt sich über 2 Cervikalseg ment und ist seh lang Im St hen od i Rückenlage enthält die Speiseröhre während der Phonatio keine Luft; i Bauchlage ist die Speiseröhre gering balloniert.

cranio-caudaler Richtung sich erstreckende Enge (Pseudoglottis) und der innere Durchmesser des Pharyngo-Oesophagus im Bereich der Pseudoglot tis war während der Phonation nur wenige Millimeter (3–6 mm) gross.

Zu Demonstration der Beziehungen zwischen Röntgenbefund und Güte der Ersatzsprache soll aus jeder der eingangs geschilderten Gruppen ein Beispiel dienen

Gruppe I

In dieser Gruppe sind Patienten in der Zeit n ch der Operation bis zum 3 post operat en Mon t. Als Beispiel sei i 71 J hre alter P tient wiedergegeben, bei dem bereits in der ersten postoperati en Phase i Bauchlage eine natomische Einschnürn g im Bereich des Oesophagusmundes na hweisba w (Abb 1) Diese dürft dem erhaltenen A t ll des M. crico-phary gleus entsprechen, der als Pseudoglottis fungiert. In dieser ersten Phase erschlucken die Patienten entweder zuwen g oder zuviel Luft. Es best ht nur in Flüsterstimm Die Luft aus der Speiseröhre wird ur für ein kurzz itige V kalisation ausgenutzt, d di Patien ten och k ine Kontrolle über den zur Sprachbildung notwendigen Luftstom haben.



Abb 2 Laryngektomierter Patient der II Gruppe Rö tg naufnahmen des Hypopharyx und Oesoph gus w hrend a) des Schluckaktes mit Bariumbrei b) I Phonati n in Tre d l nburgl g c) E-Phonati n in Seitenlag Es besteht ine erdickt hypertrophiert Pseudoglottis in Höh des 6–7 Halswi bel De Oesophagus ist sehr ng und wird nur durch ungenügende Luft gering ausg weitet Adhäsionen bedingen in Asymmetrie

Gruppe II

In dieser Gruppe sind Patienten bei denen die Operation 3–1 Monate zurück liegt Die Patienten hatten Sprechversuche mit Flüsterstimme mit 1– silbigen Wörtern ausgeführt Im vorliegenden Beispiel handelt es sich um einen 64jährigen Patienten der sich bei Sprechversuchen sehr anstrengen musste Ohne weitere Übungsbehandlung versuchte er eine Ersatzsprache zu bilden Die Röntgenuntersuchungen (Abb 2) zeigte eine in der Längsausdehnung sich über 2 cm erstre kende Pseudoglottis. Sie war in allen Lagen jedoch am besten in Kopftieflage bei E und I Phonation erkennbar Der Hypopharynx stellt eine weite Luftkammer dar und in der Speiseröhre ist eine ungenugende Windkesselbildung im Liegen und Stehen erkennbar Der hypertrophierte Sphinkter ist Folge der Unfähigkeit des Patienten die anfängliche Pseu loglottis zu relaxieren um genügend Luft in die Speiserohre zu bringen Die Hauptmenge der eingesaugten oder geschluckten Luft ist im Hypopharynx geblieben und die geringen Luftmengen in der Speiseröhre werden mit grosser Anstrengung durch die Pseudoglottis gepresst Die Prognose fur eine gute Ersatzsprache ist nicht gunstig.

Hat sich keine Hypertrophie der Pseudoglottis ausgebil let so ist die Prognose für die weitere Übungsbehandlung gunstiger



Abb. 3. Lary g ktomierter Patient der III Gruppe Röntgena fnahmen des Hypophary od Oesophagus während) des Schluckaktes mit Bariumbrei, b) A Phonation im Stehen. Die Pseudoglottis ist scharf begrenzt und fü die Sprachbildung sehr günstig Gute Luft füllung des pro imalen Oesophagus während der Phonati Di ertikelartige A sstülpu g recht m Hypophary

Gruppe III

In Gruppe III ind Patienten mit iner tad llosen Ersatzsprache Bei diesen liegt der Zeitpunkt der Operation länger ls in Jah zurück. Als Bei pi l dient ın Patient, bei dem die Operation mehrere Jahre zurückliegt und bei dem als nzugem k l Neckd ssekti erf lgt

F hand lt al h um l en 5sj hrigen Man mit der Fähigk it währe d ines Luftstoßes 10 bi 12 Silben zu sprechen Er besitzt eine ausgezeich et Sprachflüssigk t. D er Luft nicht schlu kt, sondern insaugt, hört ma k in Begl it geräusch Sein Stimmt ist gut mod liert, jedoch ge Iuso heiser wie bei iner chronischen Laryngit s. Das „A kann er 5,5 Sekunden h lten und sein Sprachgeschwindigk it beträgt 0,2 sec/Silbe Di Röntgenuntersuchung (Abb. 3) ergab in allen Positionen l en w lten Hypopharyn und inen während der Phonation al Windkessel ball förmig erw iterten oberen Oesophagusabschnitt. Di mit d m Oesophagusmund identische Pseud glotti ist scharf markiert und ihre Längsausd hnung bet ägt weniger l 8 mm, der l ere Durchmesser nur 3 mm. Als Nebenbefund best nd in taschenartige Au stülpung am Hypophary x rechts.

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TYMPANIC MEMBRANE

Electron Microscopic Observation
Part I Pars Tensa

D J LIM

From the Ol logical Res arch Lab rat ry Departm nt of Otolaryngology
Ohi State U iversity College f Medi ine Col mb Ohi U.S.A

Submicroscopi morphological d t ils of th tympa ic membrane (pars te sa) f th guinea pig, c t and squirrel monkey were st died. Three layers were disti tly recognized uter epidermal, middl lamina propria, d inner mucous. Osmiophilic da k keratin gran les, which are respo sible f keratinizati n were f und i th granula layer (strat m gra losum) i a sociati n with t nof laments—fine cytoplasmi microf laments attached t desmosomes (cell bridge) Subepidermal and submucosal con ective tissu la ers were identified on both ides f the rad t and irculs collagen u la ers. These loose connective tissue lay rs housed nerve fibers, blood vessels, fibroblast d w dering cells. Collagenous layers were composed of mixture f two types of fibrils mature coll gen fibril with dist nct xial band and finer fibril — probably prot fib ils (young form of collagen) although their xact n ture i yet t be d termined Maj r erve fibers (my linated and u my linated) were found i th sub pidermal and submucosal co nective tissue la ers, how er th ir terminals could pen trat int the epidermis. The mucou la er wa composed f single cell layer f simpl squamous ell commond t g micro illi on th ir free cell surface

Tl ere have been numerous investigati ns on the tructure of the tympanic membrane with th light microscope Th ubmicroscopic observation of this membrane—which would provide a deeper insight t ward the bette understanding of the complicated system of keratinization, cellular components, and the nature and arrangement of fibers, which could play a very important role in the formation f cholesteat ma—has not yet been av il able Thi study w s done a part of a parallel study to the xperimental

This study w done at the Electron Microscopic Laboratory Department f Otolary gology H r rd Medical School and M ssachusett Ey nd Ea I firmary nd t the Laboratory for Cell I Pathology Department of P thology Ohio Stat U i ersity Colleg of Medicine

The i estig tion w supported i part by the United States Public Health Service Research Grant No. FR-05409-06 from the N tional Institut of Health General Research Support Grant nd i part by grant from the Deafness Research Foundation.

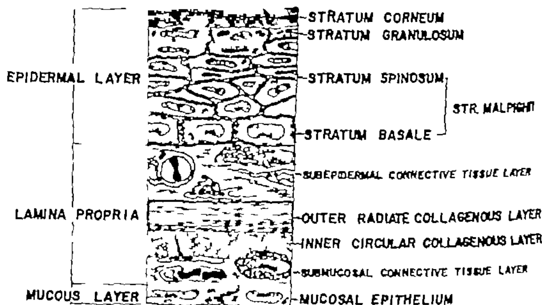


Fig 1 Cros sectional iew of th tympanic membrane (pars t nsa) f the squirrel m nk y schematically repres nted Ea h lay r i labeled in drawing

cholesteatoma currently being conducted in this laboratory This paper limits the description of the tympanic membrane to the fine morphology of pars tensa of three animal species.

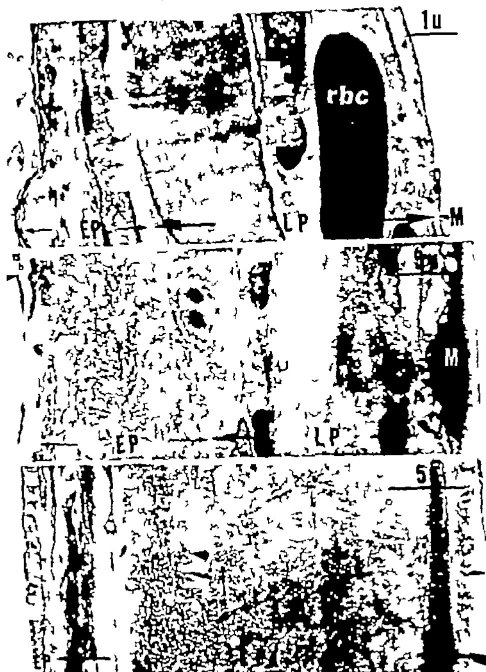
During the nineteenth century the histological structure of the tympanic membrane was described as a three layered thin membrane external cutaneous, middle fibrous and inner mucous

The middle fibrous layer was subdivided into an inner circular and outer radiate lamina (Politzer 1860 and 1892 Gerlach 1860 von Troeltsch, 1858 Prussak 1868) Toynbee (1860) believed that the tympanic membrane possessed one more layer the dermis located between the epidermis and the fibrous lamina

Shrapnell (1832) first described the pars flaccida of the mammalian tympanic membrane He stated it was anatomically different than the pars tensa and more elastic Modern textbooks do not agree on the histological description of the pars flaccida Many say that it lacks a middle fibrous layer and consists solely of cutaneous or epidermal and mucous layers (Keller 1930 Eggston & Wolff 1947 Watkyn Thomas, 1953 Bloom &

F 2 T mp ic m mbr n (central portio) f the guin pig The horny l y is xtrem ly th a d multipl lay rs of qu m o pithelium are oted in epidermi (EP) Only on lay r f coll g nou f bers cro cut, i fou d in lamin propria (LP) On the muco l er (M) ide a porti n f a capill ry with RBC is i ibl

b. Tympanic membra (a t ri r) feri peripheral portion) of the squirrel m nk y Vi ualized from left to ight are the horn la er gra ula l er nd M lpighia l r of th epidermis (EP) Lamina propria (LP) co tain g pill ry and two fibro la ers nd phagocyt s are n ted A mucou laye (M) i i uali ed o the ight hand ide of the picture with exagg rat d nterceliul pace



Tympanic membrane (anterior superior portion) of the cat. From the left, a single layer of horny cells, squamous epithelium of the epidermis (*EP*) and lamina propria (*LP*) can be seen. The lamina propria is subdivided into subepidermal connective tissue layer, outer radiate layer, inner circular collagenous layer and submucosal connective tissue layer. A single layer of mucosa (*M*) is identified on the far right side of the picture.



F a 3 H r lay nd stratum gran l um Th foll w i g structures are oted: h n l (*HL*) k rat hyalin granules (*KG*) desmosomes (*D*) d t offilaments (*Tf*)
b. A port n f th h rny l y containi g a k rat hy line gran l

Fig. 4 Survey m rograph f the heut neon l rer Arrow indicate regul rly ar ra ged n rve fibers
b. High pow r l w f nerve fiber in th bepidermal l y r Dark neurogra ules in the cytoplasm of the n rve f ber re n ted.



Micrograph showing the epidermis and subepidermal connective tissue layer containing nerve element (N). Arrows indicate the basement membrane of the squamous epithelium. In the upper part of the micrograph terminal nerves are identifiable above the line of the basement membrane (arrow). The micrograph proved that nerve terminals penetrate into the epidermis.



Fig 3 H rny l y and stratum granulos m. The f llowi g truct res are oted h rn l e (*HL*) keratohy line granules (*KG*) desmosomes (*D*) nd to filament (*Tf*)
b. A port on f the h rny l yer co taini g a keratohy l n gra ule

Fig. 4 a S rvey m ograph f the ubeut neo l yr Arrow ndi t regul rly a ranged nerv fibers
b. High power iew of a n rve fiber i th ubepidermal l yer Dark ne rogra les n the ytoplasm of the nerve fiber re n ted

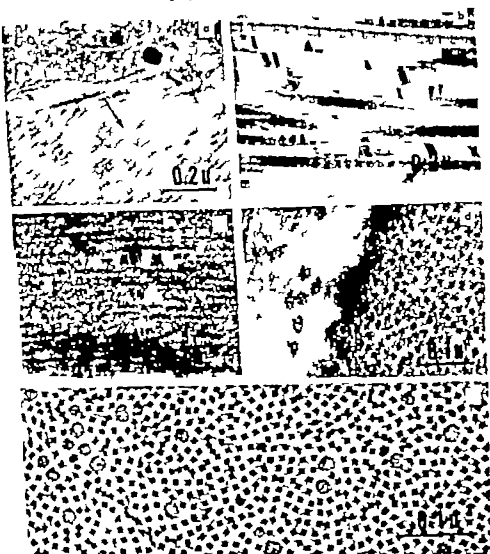


Fig. 8 Micrograph bowi g portion of fibrobl st collagen d tropocoll gen fibrils arrow T opocollagen fibril is believed t be you g f rm f collagen.
b High power iew of mat re collagen fibrils. Not regula periodic bands. It I mea ured bout 640 Å.
Long tudinal section of the fine f brils fou d i the tympa ic membrane of guine pig. X periodic bandi g could be found i the fibrils.
d. Cros sectional iew of same tympa ic membrane ( ) Obser the bundant inter f brilla m t ix.
High power iew of the cros section of the coll genous bundle f the cat. The round l rge fibril re collagen The finer fibril re rectangular

M ny investigators have discu sed the inv iv behavior of the squamou epithelial layer in wound healing nd in path logic condition uch as ch lesteal ma with some conflicting view (Habermann 1889 Bezold

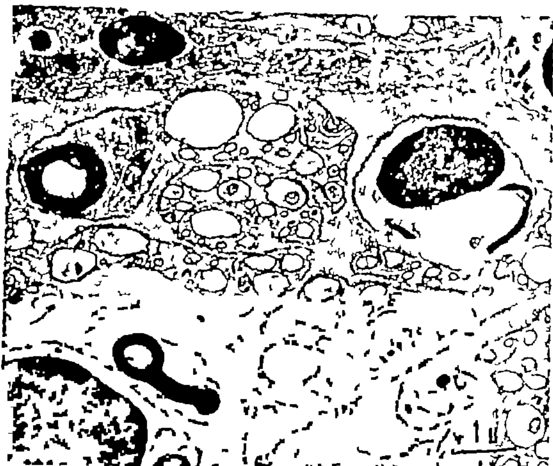


Fig. Survey electronmicrograph of the main nerve trunk near the handle of the malleus. Myelinated and unmyelinated nerves are noted. An unmyelinated nerve is encircled by a Schwann cell thereby forming mesoaxon. The upper right-hand and left-hand sides of the picture show part of phagocyte. Abundant collagen fibers can be observed between the unit nerve fibers.

Fawcett 1964). Shrapnell (1832) originally had described an arrangement of "irregular" fibers in "the middle fibrous layer". Many significant contributions concerning nerve distribution to the tympanic membrane were made at the turn of the century (Kessel 1872, Jacques, 1900, Calamida 1901, Deinike 1905, Hunt 1909, Wilson 1910). The vascular supply to the tympanic membrane was studied by Arnold (1853), Hamberger & Lindgren (1941), Saini (1963), Hamberger & Wersäll (1963).

The fiber arrangement in the fibrous layer of the pars tensa has been studied in relation to the mode of vibration of the tympanic membrane (Helmholtz, 1885, Fumagalli 1942, Secondi 1951, Kirikae 1960). The nature of these fibrous layers, in various animals as well as in human has been controversial. The muscular nature of the fibers (Home 1800) is generally denied. It is generally accepted that the fibers are collagen. Nishiyama (1 1) reported the existence of elastic fibers in humans.

Also Filogamo (1949) believed that the tympanic membrane of amphibians, reptiles and sauropsides possessed elastic and collagen fibers, while that of mammals possessed only collagen fibers.

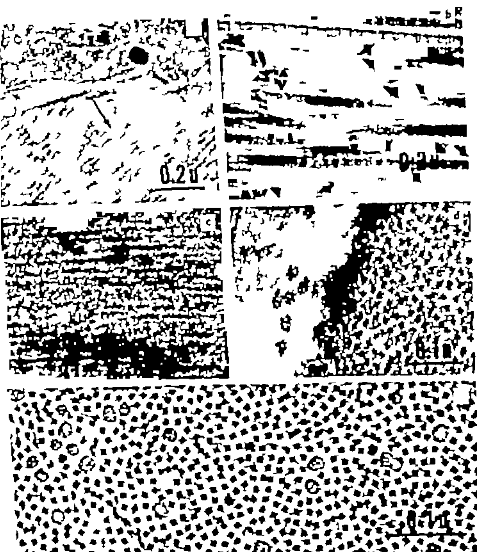


Fig. 6 Micrograph showi g portion of fibroblast collagen and tropocollagen fibril arrow Tropocollagen fibril i believed t be no g form f collagen.
b High po er iew of mat re collag fibrils. Note regular periodic bands. It is measured bout 640 Å.
Long tudi l section of the finer fibrils found i the t mpa ic membrane f gui ea pig N periodic banding could be found i the fibrils.
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Fig. 7 Ph tomicrograph of the mucou lay of the tympa ic m mbran at the transitional area betwee th membran nd middl ear mucosa Obs rve the ciliated cell (C) in the low r left hand o of the pi ture In the right hand corne the cell (Cu) has become cuboidal

1890–1 Cawthorne 1963 Rüedi 1963 Portmann 1963) Litton (1963) observed centrifugal migration of desquamating epithelium from the umbo in the normal human tympanic membrane

METHOD

Five to ten tympanic membranes were obtained from each of three adult animals of both sexes guinea pigs cats, and squirrel monkeys. The animals were decapitated and the middle ear removed from the temporal bone and immediately fixed into cold phosphate buffered osmium tetroxide (Millonig 1961) After stepwise dehydration the tympanic membrane was dissected in 70% alcohol under a Zeiss surgical microscope The complete tympanic membrane was embedded in epoxy resin (Luft 1961) in flat dishe The embedded tissue was cut in several pieces with a jeweler s saw Suitable sections were correctly oriented remounted sectioned and placed on Formvar membrane-covered grids and double stained with uranyl acetate (Watson 1958) and either lead hydroxide (Karnovsky 1961) or lead citrate (Reynolds 1963)

The Siemens Elmiscope I and the RCA EMU 2 electron microscope were used for ultrastructural observation utilizing magnification ranging from 900× to 30 000×

Cross Anatomy

Guinea pig

The thickness of the tympanic membrane (pars tensa) measured approximately 0.01 mm The shape wa almost round with a diameter of about 6 mm The tympanic membrane was suspended at the terminal portion of the trumpet shaped auditory bone It was impossible to detect a structure comparable to Shrapnell s membrane in the gross specimen and Prussak s pouch was not distinctly identified. The radiate fibers were distinct throughout the tympanic membrane (pars tensa) while the circular fibers were accumulated at the periphery and were sparse or absent at the central portion of the tympanic membrane

Cat

The thickness of the tympanic membrane measured 0.03–0 0.. mm It shape was elliptical with the largest diameter about 8 mm A distinct Shrapnell's membrane was observed

Squirrel monkey

The thickness of the membrane was about 0.02 mm and the shape was oval with diameter of 4.5 and 5.5 mm A distinct Shrapnell's membrane was present with an occasional mucosal fold on the back side of the membrane The general anatomy of the tympanic membrane of this animal was similar t that of the cat.

Electron Microscopic Obs rvation of the Pars Tensa

Epidermis

The epidermis is divided into (1) stratum corneum, (2) tratum granulosum, nd (3) stratum Malpighii, which is subdivided into stratum spinosum an l tratum bas le (Fig 1)

Stratum corneum i the outer l yer of the epidermis and consists of several layer f compressed, almost acellular structures. *Keratohyalin* pigments were observed lying in a rather dark homogeneous strip near the basal portion of the corneum, and they appeared similar to the *kerato-l yalin* pigment f und in the adjacent stratum granulosum *The remnant* f desmosomes between these stacks of horny layers were still observabl even when they were extremely flattened (Fig. 3 b)

Stratum granulosum i directly underneath stratum corneum and consists f one or two cell layers, characterized by abundant dark keratohyalin granules. Th ize of the granules, irregular in shape varied from 0 1 to 1 µ The cytoplasm f thi gr nular cell wa less electron dense du to a reduced amount of cytoplasmic tonofilam nts than the cells in the Malpighian layer howev r microfibril were still present in appreciable mount Very close contact between keratohyalin granules and tonofilaments was con tantly observed, yet the actual aggregation of the keratohyalin wa



FIG 7 Ph t micrograph of th mucous lay of th tympanic membra e at the transitional area between the m mbran nd middl ea mucosa Obs rve the ciliated cell (C) in th lower l ft hand corner of th picture In th right hand corn th cell (Cu) ha becom boidal

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not clear (Fig. 3 a) The other cytoplasmic contents included a small Golgi apparatus, small elongated mitochondria and scattered, rough-surfaced endoplasmic reticula. Overall, the cell was flat with a flattened nucleus and the interdigitation of the cytoplasmic membrane observed in the Malpighian layer was not present in these cells.

Stratum Malphigii is subdivided into two layers stratum spinosum and tratum basale

Stratum spinosum is composed of three to eigl t layers of squamous cells in cats and squirrel monkeys but in guinea pigs only three to four cell layers. In this layer the intercellular pace was more readily noticeable than in tratum granulosum however the cells nearest to stratum granulosum were more compressed than the cells nearer to stratum basale and showed xtreme condensation of cytoplasmic content with a diminished inter cellular space. The nucleocytopla mic ratio of these cells was high compared to that of the epithelial cells in the mucous layer. The cytoplasm contained bundant tonofibril (microfibril) These were in general, oriented parallel t the longitudinal plane of the cell and in some cases attached to the desmosomes. Abundant RNP particles and some lamellar endoplasmic reticula were observed. Desmosomes—consisting of two local thickenings of the cell membrane and three extracellular lamellar structures between two thick ned membranes—occurred abundantly along the border of the squamous cells. They appeared to serve as a tightening apparatus which bound each cell together

Stratum bas le the innermost layer of the epidermis, consi ted of a single layer of cell It is separated from the connective tissue layer by a basement membrane. The shape of this cell in the squirrel monkey was nearly cuboidal but in the cat and guinea pig it was flat. In the guinea pig the cell possessed long processes. The nucleus was sometimes infolded and had a high nucleocyt pla mic rat The cytoplasm contained small, elongated mitochondria abundant lamellar nd rough urfaced endoplasmic reticul and m derat amou nt f ton filaments. The hemidesmosome seen in the *monk y and cat wa not identified* in the guinea pig (Fig 2 a)

Lan n pr pri

Th lan in propria i ubdi ided into 1) *subepidermal connecti e tissue* laver 2 ra l t collagenou b ndle laver 3) *circular collagenou* bundle laver nd 4 ubmucosal connective ti sue layer (Fig. 1)

The subepidermal connect e ti sue layer i composed of loose collagen fibers, f br blasts, nerve fibers (mostly unmyelinated xcept f r the peri pheral p rt in f the tympanic membrane and along the handle of the m ll u d capill ries. Un y linated nerve fibers accompanied the capill ri es, but actual nerv contact with the capillary wall wa not clea ly dem n tr ted There wa con incing evidence th t there are w ll arranged nerv fibers in thi layer (Fig. 4 a) Neurosecretory granules, neur fila-



F a. 8 Sk l of the t mpanic membrane Granular cell (G) basal cell (B tratum pin m (S)

b Photomi rograph f th lami a prop la and m cosal cell Lam na prop l (LP) radial fibe (/) ircula fiber l ross secti n l iew (/) fibrobla t (F Schw nn cell (S) ne re fibe (n) mucou m mbra (mm)

included well-developed lamellar endoplasmic reticula, Golgi's apparatus and small mitochondria. They did not include tonofilaments, keratohyalin granules or secretory granules.

DISCUSSION

The lamina propria (middle fibrous or collagenous layer) is the most complicated and controversial layer in the tympanic membrane. It has been generally accepted that the lamina propria is solely composed of radiate and circular fibrous layers, although Toynbee (1860) had described the dermi of the tympanic membrane as a distinctly independent layer of connective tissue located between the epidermis and fibrous layer. However he failed to recognize a thinner but identical layer between the mucosal epithelium and fibrous layer. Later Bloom & Fawcett (1964) described th layer as lamina propria of the mucosa" These loose connective tissue layers contained blood capillaries, nerve fibers, fibroblasts, lymphocytes, phagocytes and mesenchymal cells.

The fibrous bundles in the lamina propria are generally believed to be composed of collagen—possibly with elastic fibers. My materials suggested th t there may be pecies differences. The lamina propria of cat and m nkey possesses collagen fibrils intermixed with finer fibril which form multiple fibrilla bundles. However in guinea pigs only finer fibrils without distinct axial band were noted which suggests a different type of fibrils than collagen.

There was some similarity between the finer fibrils of cat and guinea pig (in cross sectional views) suggesting that they may be the same. The unit fibrils w re composed of four subunits forming a rectangle in cross sectional view. The nature f these finer fibrils is yet to be determined with hi tochemical means. Although, Hamilton (1967) described four subunit fibril in the a sociated fibrils of perilymphatic fibrocytes of the vestibule nd h suggested these might be keratin fibrils on the basis of other investigators data (Bairati & Iurato, 1959 Iurato, 1962).

Porter s investigation on lamprey skin (1964) showed a wider range of caliber in unit collagen fibril (30A–600A) and he found that fine protofibril (y ung f rm of collagen fibrils) were located very near to the fibroblast and mixed with mature collagen fibrils which was true in the subepidermal nd ubmucosal connecti e tissue layer of the tympanic membrane. Exi tence of lastic fibers requires further investigation before definit conclu ion are drawn. This is because of the varied appearance in lectron microscopic examination. Even in fibrillar form it lacks an axial periodic band which allows it to be differentiated from collagen fibrils (Porter 1964 Freeman, 1964 Gotte *et al* 1965).

The tympanic membrane is one of the most sensitive parts of the body and m ny investigators have studied its nerve distribution and nerve terminals. Wilson (1907) believed that the main plexus was a wide-meshed

ments, and neurovesicles in the unit nerve fiber were present (Fig. 4b) The major nerve plexus was chiefly limited to this connective tissue layer but a structure resembling a free nerve ending was observed between the squamous cells of the epidermis (Fig 4c) In the cat occasionally a twisted rope like bundle of nerve fibers was found Each unit fiber was encircled by the Schwann cell membrane Both myelinated and unmyelinated nerve fibers were found at the peripheral portion of the tympanic membrane and at the margin of the manubrium Frequent local dilatations of a unit fiber (unmyelinated nerve) were observed along its long axis however synaptic structures were not evident A clear demarcation between this layer and the adjacent radiate collagenous layer was not observed

The fibers of the subepidermal connective tissue layer consisted of typical collagen fibrils and protocollagen fibrils (Fig 6a and b) The fibers of the radiate and circular collagenous bundle layer were mainly composed of finer fibrils in guinea pigs and cats In the squirrel monkey the diameter of unit fibrils varied from 50 Å to 600 Å

The finer fibrils frequently appeared rectangular with four subunits in cross section one edge of the rectangle measured approximately 50 Å In longitudinal section the periodic bands were not observed (Fig 6c d and e) However in the case of cat a few collagen fibrils with diameter varying from 400 to 600 Å were intermixed with the aforementioned rectangular fibrils Homogeneous interfibrillar ground substance was observed in all animals

The circular collagenous bundle layer was identical with the radiate layer except for the arrangement of the collagenous bundles, which was at a right angle to the former and thinner This layer poorly developed toward the center portion of the tympanic membrane was sometimes entirely absent

The submucosal connective tissue layer was identical with the subepidermal connective tissue layer except that it was thinner It was comprised of nerve fibers, capillaries, loose collagen fibers, fibroblasts, and occasional wandering phagocytes (Fig 2b) and it bordered with the mucosal epithelium by a basement membrane The distribution of nerves and capillaries was more sparse than in the subepidermal connective tissue layer and the free nerve endings did not appear to penetrate the mucous layer

Mucous layer

The mucous layer was composed of simple squamous epithelial cells except that at the margin of the tympanic membrane it was composed of cuboidal cells sometimes with and sometimes without cilia (Figs 7 and 8b) The cells of the mucous layer were basically flat although some may have been cuboidal at the margins with a rather high nucleo-cytoplasmic ratio

These cells had microvilli on their free cell border prominent pinocytotic vesicles and interdigitating plasma membranes The cytoplasmic contents

included well-developed, lamellar endoplasmic reticula, Golgi's apparatus and mall mitochondria. They did not include tonofilaments, keratohyalin granules or secretory granules.

DISCUSSION

The lamina propria (middle fibrous or collagenous layer) is the most complicated and controversial layer in the tympanic membrane. It has been generally accepted that the lamina propria is solely composed of radial and circular fibrous layers, although Toynbee (1860) had described the "dermis" of the tympanic membrane as a distinctly independent layer of connective tissue located between the epidermis and fibrous layer. However, he failed to recognize a thinner but identical layer between the mucosal epithelium and fibrous layer. Later Bloom & Fawcett (1964) described thi layer as "lamina propria of the mucosa". These loose connective tissue layers contained blood capillaries, nerve fibers, fibroblasts, lymphocytes, phagocytic and mesenchymal cells.

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one in the fibrous tissue through which most of the fibrils passed to form a subepithelial plexus under either the epidermal or mucous layers. He described various types of nerve endings. My observation did not add much to his description. The ground plexus was located in the subepithelial connective tissue and gave off branches to vessels. The subepithelial plexus to the mucous layer was located in the subepithelial loose connective tissue layer and formed free nerve endings. The major nerve trunk found along the manubrium was composed of myelinated and unmyelinated nerve fibers.

Also there were myelinated nerve fibers at the periphery of the membrane. I observed a nerve structure in a cat which was regularly arranged in intervals. The distribution of free nerve endings in the epidermal squamous cell needs more study. In squirrel monkeys, it was observed, the free nerve endings seemed to penetrate the epidermis.

My findings of the blood vessels of the tympanic membrane agree with those of Politzer (1892) who described two plexus. These capillaries were located either in the subepithelial connective tissue layer (external plexus) or in the submucosal connective tissue layer (internal plexus) and were accompanied by unmyelinated nerve fibers (possibly sympathetic fibers).

The outermost layer of the tympanic membrane is the keratin layer similar to that of the skin. Keratinization is a synthesis of protein and lipid in desquamating epithelium. Since the external surface of the tympanic membrane is a continuation of the external auditory canal skin, it is conceivable that the basic desquamating and keratinizing processes are the same. This complex mechanism of keratinization is beyond the scope of this paper; however, I feel that this important cellular dynamic renders deep insight toward the understandings of the physiology and pathology (cholesteatoma) of the tympanic membrane. Therefore it may be of interest to review the basic principles of keratinization for our better understanding of underlying problems.

Most investigators are generally in agreement that the tonofilaments of epithelial cells are closely related with keratohyalin granules (precursor of *cholesterol ester) in the cells of stratum granulosum.*

How these granules aggregate, however, is still debatable (Rhodin & Reith, 1962; Brody, 1960; Odland, 1964). In the experimental study it was found that keratinization of the epidermis depended on the type of mesenchyme with which it was associated (McLoughlin, 1961; Wessels, 1962). *In* McLoughlin's study he attempted to combine isolated chick embryonal epidermis with various tissues, and found that when enclosed by heart fibroblasts it formed an islet of thick squamous epithelium which keratinized even more extensively than epidermis *combined with normal dermis.*

Another interesting aspect of the epidermis is its ability to maintain the same thickness even with continuous shedding of the horny layer. The perfect equilibrium—a balance between proliferation of epidermal cells and desquamation of horny cells—is maintained by a sensitive feed back

mechanism This fine regulatory mechanism determines whether a newly f rmed cell in the ba al layer will divide mitotically or will differentiate int a horny cell which will eventually be shed as a single cell (Bullough, 1962) It is well documented by Pinkus (1938) that when human epidermis is grown in vitro, only the basal layer survives and grows. This indicated all the other cell are post mitotic" It is interesting to know that the mitotic activity could be influenced by certain stimulations—such as rem val of the horny layer (Pinkus, 1951 1952) and hormones (Eartly *et al* 1951)

Another interesting observation was that the basal cell in the epidermis showed difference among the species. Basal cells of the guinea pig did not possess hemidesmosomes, while in monkeys and cats hemidesmosomes were very distinct at the base of the cell where the cell makes its contact with the basement membrane

The bi logical meaning of the absence of this structure in the guinea pig wa not quite clear The mucosal epithelium (simple squamous epithelium) was morph logically identical with that of the mucosal epithelium found in th middle ear mucosa in the author previous study (Lim *et al* 1967) nd the secretory granules found in the middle ear mucosa were not identified in the mucosal cell of the tympanic membrane

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ZUSAMMENFASSUNG

Die orliegend Arbe t bef st ich mit de lektronenmikroskopischen Unter suchu g morph logische Deta ls der Pars tensa des Trommelfelles beim Meer schw nchen, be der k tze beim Affen (Saimiri sciurea) D bei kon ten drei erschied ne Schi ht klar unterschieden werden ine äussere Ephidermisschicht ein m ttlere Laml prop ia und ine innere Schleimhautschicht. Osmioph le dunkle Keratingra la die für den Verhornungspro ess erantwortli h si d, finden si h m Stratum granulosum zusammen mit sog. Ton filamenten, (la ytoplasmatischen Mikrof sern, die mit Desmosomen (Zellbrücken) i Verbindung st hen. Zu beiden Seiten der radiären und zirk lären K llagen schichten nd subepidermale bzw submuköse Bindegewebsschi hten geord et,

Diese lockeren Bindegewebsschichten beherbergen Nervenfasern Blutgefäse Fibroblasten und Wanderzellen Die Kollagenschichten setzen sich aus zwei Arten von Fibrillen zusammen aus reifen Kollagenfibrillen mit deutlichen Achsenbändern und aus feineren Fibrillen wahrscheinlich Protofibrillen (junge Formen von kollagenem Bindegewebe) die genaue Natur letzterer muss jedoch noch bestimmt werden Grössere Nervenfasern (markhältige und marklose) finden sich in den subepidermalen und submukösen Bindegewebsschichten ihre Endfasern dringen jedoch bis in die Epidermis vor Die Schleimhautschicht besteht aus einer einzigen Lage von einfachem Plattenepithel mit Mikrovilli an der freien Zelloberfläche

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SQUIRREL MONKEY RAIL TEST

A Design for Testing Dynamic Equilibrium

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The squirrel monkey (*Saimiri sciu eus*) rail test, whi h i based on the avoidance co ditioning method is designed to detect the disequilibrium that is exhibited by h nge i locomotor performance The present procedure m kes it possible t obt in quantitati e and comparable data, d t compare compensati n pattern after selecti ablation of dif ferent part f the estibular system i subhuman primates. Th re-presentati dat from several different groups (ilateral labyrinthec t my unilateral utricular nerve secti n unilateral saccular macula de-struction nd unilateral stapedectomy) were presented to comp re the ffect of ea h surgi l proced re upon the performance of squirrel monkey rail tests.

The vestil ular system is considered to have two modes of function first to receive ny sort of stimulation (usually the nature of mechano-stimulation) to the end org ns, o to the neural pathway itself and to exhibit a sy temic reaction t the stimulation and, second, to contribute to the maintenance of both tatic and dynamic bodily equilibrium in ordinary daily life The latter is supposed to be the more natural function of the vestibular ystem nd the importance of the estibular system in posture and locom tion i well described both physiologically (Magnus, 1926 Birren, 1945 Löwen tein, 1950 1956 Wendt 1951 Gernandi, 1959 1961) and anatomically (Lorente de N , 1933 Carpenter 1960 Brodal *et al* 1962 Nyberg Hansen, 1964 Nyberg H nsen & Mascitti, 1964)

The role of each different part of this system in maintaining bodily equilibrium is n t yet clearly known. An attempt wa made to investigate quantitati ely th contributi n of each indi idual part of the vestibular s tem with respect t it function in maintenance of bodily equilibrium. In the present study the est bli hment of the squirrel monkey rail test which will permit the quantitative measurement of dynamic disequilibrium (left-right) was the first ta k undertaken and will be described first. All ablation experiment will be reported subsequently

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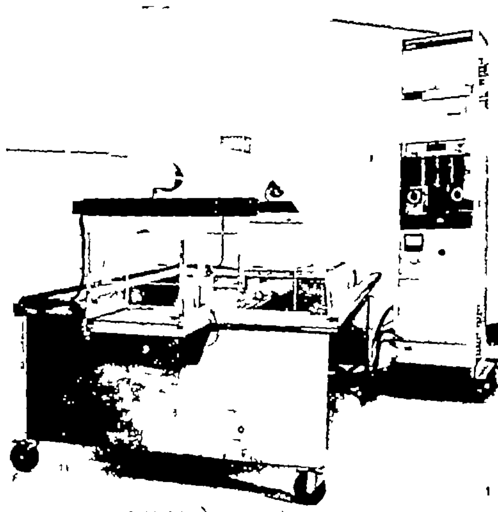


FIG 1 Squirrel m nk y rail test cage d operating pa l which includes m ster control pan l powe supply unit hock pow supply and control, and th rs

Squirrel monkeys were chosen because they are subhuman primates and are extremely suitable for a behavioral conditioning program They are inexpensive, and also of all the experimental primate family they are the easiest to handle and maintain All animals were quarantined upon receipt for a minimum period of two weeks before their use

A picture of the basic apparatus used in this experiment is shown in Fig 1 Its dimensions are 6 ft long, 4 ft wide and 4 ft in height the top 28 inches being constructed of $^1/_4$ inch thick transparent plexiglas Extending beyond each end is a plexiglas box (1 × 1 × 1 $^1/_4$ ft) equipped with sliding doors The lower part of this apparatus is constructed of steel This is to be referred to as the tank Electric shock grids are mounted on the floor of the tank and on the floor of each end cage Over each end cage is mounted a light bulb which acts as a signal Inside the tank about 3 inches below the base of the end cages, in the center of the tank and extending horizontally the entire length of the tank is a 1 $^1/_2$ inch wide cross-shaped rail which can be rotated A piece of plexiglas shield installed at the opening

of each box allows only enough room for the animal to walk across the rail and not to jump from one of the boxes to the other. A large piece of blackout suede cloth covers the entire apparatus, with a small hole through which the examiner observes. The room should be darkened always.

Mounted at one end of the tank is a 1/ h p D C motor the belt of which rotates the rail. This motor is powered and controlled by a power supply which enables the examiner to choose any rpm within a range of 0 to 1000. The panel which operates this apparatus automatically consists of 1 master control panel, 1 digital recorder, 1 electric counter, 1 indicator panel, 2 timers, 1 switch panel, 1 shock power supply and control, 1 response counter, 2 sequence alternators, 1 grid shock scrambler, 1 motor speed control unit, and 1 constant voltage D C power supply.

PROCEDURE

Basic Settings and Maneuvers

When the main power switch for the apparatus was placed in the "on" position, the entire apparatus was activated except for the rail rotation. The light over one box was turned on, while the light over the other box remained out. The Shock Device, which supplied voltage to the grid in the tank and to the grid in the darkened box, was turned on. Thus, the light would act as a safe signal for the subject. The shock intensity could be manually controlled by the examiner. The rail was rotated at a low speed (50–100 rpm). The sliding door at the entrance of the tank was closed to prevent the subject from entering. The subject was then transferred into the lighted box from the end and after a certain time period, the sliding door was removed. Ample time was allowed for the subject to become accustomed to the new surroundings, after which the timer that controls the light was activated. At the end of 13 seconds, which is the interval between light alternations, a sequence alternator turned the light off at the one box where the subject was waiting and switched it to the other box. The shock was turned off simultaneously at the far end box. As this occurred, the shock timer was activated and run for 2 seconds to count the interval from light out to shock. When this time had elapsed, the second sequence alternator turned the shock on in the darkened cage. During the 2 second interval period, no shock was on in either cage. If the subject failed to respond during this interval, he received a mild electric shock of manually controlled intensity. The current flow through the grid on the floor of the tank was on constantly during screening and training periods (manually controlled intensity) so that any time the subject stepped down onto the grid, he received a shock. Each time a cycle (or 1 trial) had been completed, the counter recorded it. At the end of the session the timer was stopped, the plexiglas door was replaced, and the subject was removed from the lighted cage.

Screening

The animal was placed in the lighted cage Ample time was given for the subject to adjust to the new environment the slowly turning bar noise of the motor shape of the apparatus and so on After the subject had adapted to the surroundings the plexiglas obstruction was removed. The animal would explore the apparatus discovering the electrified grid in the darkened cage and in the tank After learning there was no outlet, he finally came to rest in the lighted safe cage Again time had to be given for readaptation Thereafter the "light off—2 seconds—shock on" schedule was started with a 15 second or more interval Twenty trials were usually given to the subject and positive responses were counted The purpose of the screening had to be left to the elimination of the unfavorable subjects for the rail-crossing behavior conditioning Daily sessions for about three days were required for most individuals before reaching the decision The animals which showed more than 90% of good performance on their third screening day were usually considered to be acceptable animals The extremely nervous and excitable animals had to be eliminated even if they made good scores, as most of them would have become inadequate sooner or later In addition monkeys which demonstrated malperformances, such as stepping down onto the grids, or stopping and turning with the rail, or jumping onto the rail were eliminated from the program

Using this basic screening method only the most appropriate animals for rail-crossing behavior conditioning were selected The rate of discard during the screening and training procedures was 17 7% among the latest 51 animals. After the completion of screening and training only a few monkeys were discarded (because of malperformances as described above) during the period of threshold measurement The rate of discard was 9.8 among the recent 51 animals

Training

The animals chosen had to be trained to demonstrate the correct response every time and preferably to avoid the shock The rail had to be rotated up to about 200 rpm A daily training session using 15-second intervals between light alternations and 2 second intervals between the light and shock was used For the first two days, a training session of about 15 minutes was used After this period the sessions could be lengthened The subject then practiced for the successive days, making a total of about 5 (preferably 10) training sessions. This was considered to be adequate time to train the animal well

Threshold Measurement (Pre- and Postoperative)

After the basic training the animal was then scheduled for preoperative threshold measurement Threshold was the highest possible rpm at which

the subject could traverse the rail without falling. Since basic training was performed at about 200 rpm the examiner began preoperative threshold measurement around this level The examiner then increased the speed f the rail in increments of 50–100 rpm The examiner observing through the small hole in the blackout cloth recorded the results of each response the ubject made Increa es in speed of rotation in 50-rpm increments were made until the subject made his first fall The rail rotation remained at this rpm allowing the subject 2 more times to cross. If the subject fell 3 consecutive times, this was considered as threshold for that day s per formance However if he fell, f r example only once out of the allotted 3 tri ls, the speed was increased another 50-rpm increment If the subject f ll 2 f the 3 all tted trials, the speed of the rail still had to be increased an ther 50 rpm It was only when the subject fell 3 consecutive times at a given rpm that the threshold was decided f r that specific day (Figs 2 a–d)

F r several days, after the initiation of the preoperative threshold measurement the threshold increased It was usually after 3–4 days that the daily preoperative thresh lds became more stable, formulating the final threshold The criterion for the fin l performance threshold was that the animal had to maintain the same daily thresholds for a minimum of 3 (preferably 5 r 6) consecutive days. Most of the subjects exhibited steady d ily consecutive thresholds h wever In some cases, a 50–100 rpm varia tion among the daily thresh lds was permitted while deciding the per formance thre hold. After the minimum of 3 consecutive thresholds was attained, the animal was r ady f r surgery or for any sort of experimenta tion

The first postoperative threshold measurement wa performed twenty t tw nty four hours aft r the operation, a it was found that in this pecies there wa n direct effect from the general anesthesia at this time. (Thi will be discussed later) Postoper tive threshold measurement was d termined a before nd foll wed a pattern similar t preoperative thresh ld determinati ns. The increment increase was also 50–100 rpm however thi had to be st rted u u lly from 0 rpm

In addition to the tl resh ld measurements, the analysis of the daily trial pattern wa perf rmed in order to acquire more accurate indication of lynamic lisequilibrium

Surgery

All urgery wa performed under general anesthesia produced by the intra enou injection f sodium pentobarbit l (30 mg/kg)

Th urgical procedure f saccular macula ablation will not be described in det il ina much a it is not the purpose of thi report to outline the det il of each different ablation procedure Thi information will be pre sented in ther reports.

A r transauricular approach w used in tead of the inferior approach used

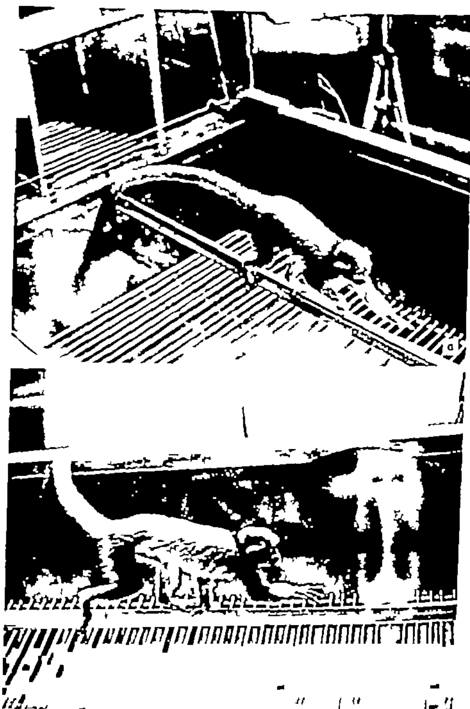
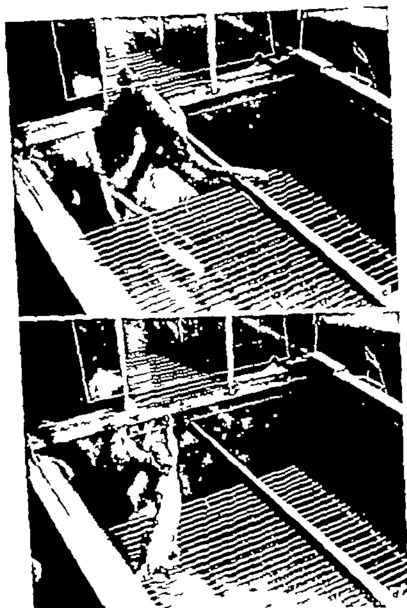


Fig. 2. Photograph demonstrating the squirrel monkey performance in the rail cage a and b. The monkey is traversing the rail. The vision is fixed to the target which is located straight ahead, and not to the rail itself. The monkey is reaching the safe corner (light-on) d. The monkey failed to complete traversing the rail. Well trained monkeys usually do not require any look when the thresholds are measured.

for rabbits by Versteegh (1927) and Jongkees (1950) and the greater part of the operation was performed under the operating microscope. After retracting the external canal skin and tympanic membrane forward the posterior superior bony canal wall was removed by a small angled curette



After exposing the middle ear ca ity the chorda tympani nerve wa di ided. The incu wa u nally removed after subluxating the incud stapedial joint with fine pick to obtain better vi ibility of the ov l window area. The tapedial tend n was divided nd the annular ligament of the tapes was separated all around the footplat by a very fine pick Attempt were made t r move th tapes in t to however some were removed in a piecemeal m nner During thi proced re intense m vement of perilymph was strictly avoided. F r the t pedectomy control gr up the overall e procedure was

stopped at this point For the other control group of saccular membrane rupture only (to be discussed in another report) an extreme fine pick was inserted through the oval window to rupture the saccular membrane without destroying the otolithic membrane or the macula For the saccular destruction group however the procedure was extended in that the anteroinferior edge of the oval window was drilled off a little to acquire a better view of the entire saccular macula The saccular membrane was ruptured and a fine pick was used to remove the otolithic membrane and to destroy the saccular macula The rupture and dislodgment of the otolithic membrane had to be ensured during this procedure so that the saccular macula carried no more otolithic end organ function (Jongkees & Philipszoon 1964 James, 1962 Igarashi 1965) The use of suction was strictly minimized during this entire procedure, except for removing bone dust and blood Thereafter the oval window was sealed by autogenous soft tissue graft (fat in most cases) which was kept in place by gelfoam in the tympanic cavity The canal skin flap was replaced and the incision closed Postoperatively 50 000 units of potassium penicillin G were injected intramuscularly

Histological Confirmation

Histological confirmation of the surgical lesions is most important Animals were sacrificed after complete or satisfactory recovery of equilibrium however the time of sacrifice depended entirely upon the experimental purpose The animal was intravitally perfused with Heidenhain-Susa solution Temporal bones were further fixed in the same solution under refrigeration After being decalcified by 20% DECAL solution or 5% tri chloroacetic acid for an average of three weeks or slightly more, the specimens were proceeded to washing, to 5% sodium sulfate solution to rewashing, and thereafter to dehydration with ethanol All specimens were embedded in celloidin and serial horizontal sections were made at 20 microns thickness The sections were stained in Hematoxylin Eosin and examined by light microscopy

EXPERIMENTAL DATA

General Anesthesia Controls

Sodium pentobarbital 30 mg/kg was injected intravenously for each control animal Control animals were tested 20 to 24 hours after injection which is the standard procedure for operated animals Ten out of 13 control monkeys receiving only anesthesia without surgery did not demonstrate any change in their threshold values and patterns of rail-crossing performances, while the other three showed 50–100 rpm change in threshold which is still within the normal range Animals that had a 50–100 rpm decline returned to a normal threshold within the next 20–24 hours It is therefore



FIG. 3 a. Photomicrograph demonstrates normal i ner end orga fter routine st pedectom proced re Not intact ot lithic membrane on macula sacculi. Macula t iculi nd semicircula duct cristae were ll i tact.

FIG. 3 b Photomicrog ph xhibit the les f saccul macula destruction. Not the macula l les ted from the bon w ll (arrow) nd no ot l thic membrane i seen. Ma bon chips, which could be seen in the saccular recessus, indicat that the rea scraped off by pick Macula tricul nd semicircular duct rista were morphologic lly intact.

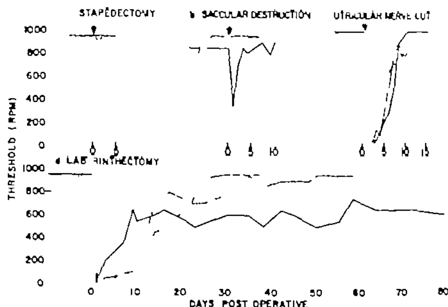


FIG. 4 Graphs demonstrate different threshold declines and compensation patterns among the groups with different unilateral operations, routine stapedectomy, saccule macula destruction, utricular nerve cut and labyrinthectomy. Changes in performance patterns are not demonstrated in this figure.

reasonable to assume that in most animals the effects of intravenous sodium pentobarbital injection does not exist when the threshold performance is measured 20 to 24 hours after the injection. This is also confirmed as the postoperative thresholds did not decline in most of the cases with sham procedures.

Surgical Ablations

Inasmuch as it is not the purpose of this report to discuss in detail the roles of different parts of the vestibular system contributing to equilibrium, representative information from several different groups will be presented (Figs. 3 a–b and 4).

To date the saccular ablation group has demonstrated the largest intra-individual variation in postoperative threshold declines (although the compensation patterns are similar) and the other groups show much less intra-individual variation. Although twenty-two squirrel monkeys had saccular ablation utilizing the same surgical procedure, they still exhibited the largest intraindividual variation. Details of this saccular ablation study will be discussed in subsequent reports.

The differences in the postoperative threshold declines and in compensation (recovery) patterns among different groups are significant (Fig. 4). All cases were operated unilaterally. The labyrinthectomy group exhibited the greatest effect from the operation, requiring one to two months to regain preoperative threshold. One case failed to regain the preoperative

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threshold even three months after surgery. The utricular nerve section group showed more significant effect than the saccular destruction group, although the compensations were rather unexpectedly fast. The animals with utricular nerve section required ten days or m re to regain preoperative threshold while those with saccular destruction regained their preoperative thresholds within five days postoperatively. The monkeys with stapedectomy only failed to demonstrate any significant threshold change postoperatively.

DISCUSSION

In man, many tests have been designed analyzed, and extensively evaluated in an effort to examine the influence of vestibular function in the maintenance of dynamic bodily equilibrium (Hirsch, 1940 Fukuda 19 9 a 1959 b 1961 Jordan, 1963 Zil troff-Pedersen & Peltersen 1963 Peltersen 1963 1964 1967 Graybiel & Fregly 1966) however as basic animal experimentation considerably few studies to corroborate their observations have been made.

Maier (1935) and Furchtgott & Echols (1958) devised the performance test for measuring locomotor coordination in rats (cortically ablated and x-irradiated) by requiring them to traverse two parallel narrow bars a certain distance. They have demon trated their data in a quantitative fashion. In 1961 Cohen designed the gymn sium which includes pegboard, erhead horizontal l dder trapeze vertical ladder and vertical pole f r the investigation of mot r coordination in primates by using the behavior (reward) conditioning technique. Only the qualitative data was obtainable by his method how ver.

The present squirrel monkey rail test which is based on avoidance con diti ning methods, is con idered to be a combination of these different animal locomotor perf rmance tests. The advantages of the present method are quantitative and comparable data are obtained, and compensation pattern can be compared, fter ablation of different selective part of the vestibular system in subhuman primates. Because of the *unilateral operation, th present monkey rail test mea ures left right disequilibrium* of tr ined locomotor conditions with other normal ones, resulting from different ablation procedures.

The subject in the present tudy are not equal to the n rmal rand m samples because all unsuitable animal were screened out originally as previou ly described here and a in the cat behavioral conditioning auditory tests (Schuknecht, 1953 Igarashi & Hoyt, 1963). Threshold performances require locom tor practice under full alertness therefore the performances d monstrate locomotor trained condition. However all animal were trained and the threshold measured by using identical m thod and with extremely few exceptions, most monkeys had easily reached the 900–1000 rpm threshold l vel. Thi method, therefor is not limited to highly killed

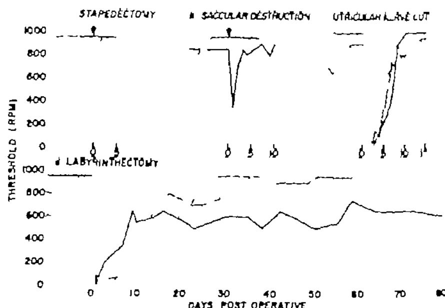


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Gratitude is ext nded t D J S. Thach J Dr B. R. Alf rd Dr A Graybiel, Dr F R Guilford, and Dr D Riccio for their productive suggestions, constant encouragement and support.

RESUME

Le test d rail avec les *Saimi i sciureus* (squirrel monkeys) basé sur la méthod de conditionneme t pour action d éviter est désigné à découvrir le déséquilibre qui se m tre en ha geant l'a tion locom t ice A ce le procédé actuel il est possible d'obtenir des don ées quantitatives et comparables et de comparer les dessin d comp nsation après ablati n sélective de différentes parties du système estibulaire dan des primates presque humains. Les do nées, représe tant plusieurs groupes différentes (unilatérale labyrinthectomie unilatérale utriculaire section d nerf, u ilatérale sacculaire destruction d maculae et un latérale stapedectomie) fure t présentées pour comparer les ffets d chaque procédé chirurgicale sur le fonction ement des *Saimiri sci reus* dans le test d rail.

ZUSAMMENFASSUNG

Der uf der Verm idu gs-Bedi gungsmethode basierende Schienen ersuch mit *Saim ri iureus* (Totenkopfäff hen, squirrel monkey) wurde entworfen um den Glei hgewichtsverlust, der sich d rch inen Wechsel in der lok mot ren Leistungsfähigk t zeigt zu entdecken Die gegenwärtige Arbeitsweise ermöglicht es, quantitative und erglelchbare Daten zu erhalten sowi in subhumanen Primaten Kompensati nsmuster nach selekt ver Beseitigung verschiedener Teile des vestibularen System zu vergleichen Di bezeich enden Daten von mehreren verschieden Gruppen (inseitige Laby inthektomie inseitige utrikulare Ner vensektion einseitige Zerstöru g der Macula sacculi und inseitige Staped k tomi) wurden vorgelegt, um d Eff kt eines jed n chirurgischen Eingriffes auf die Ausführung der *Saimiri-sci reus* Schienenversuche zu vergleichen.

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individuals It may not measure quite the same thing, however as in human subjects by the rail walking test

All sham surgical procedures were done stepwise so that should any part of the procedure create a change in threshold of monkey performance chances were better for early detection of such change. For the saccular ablation group for example general anesthesia controls, stapedectomy controls, and saccular membrane rupture (no macular destruction) controls were studied so that the results obtained after saccular ablation were critically analyzed

Histological confirmations were done not only after recovery of functional performances but also at the time of greatest postoperative threshold decline (first day after surgery) in two or three cases from each group By doing this both acute and chronic histology were investigated comparatively in each ablation technique The original purpose of the histological confirmation of selective end organ ablation was to investigate how completely that particular end organ was destroyed, and to confirm that no other end organ was involved morphologically therefore the contribution of that particular end organ toward maintenance of equilibrium should be determined

From the representative data of different surgical procedures, it was confirmed that labyrinthectomy had the severest and most prolonged effect One out of three in this group did not even regain the preoperative threshold level after surgery This is most probably due to the fact that surgical destruction was done so extensively (possibly involving the neural system) that the disequilibrium was beyond central compensation

It was also very clearly demonstrated that the macula utriculi contributes more than the macula sacculi does, to the maintenance of dynamic equilibrium More significant threshold changes and longer compensation periods were observed after utricular nerve section

The difference between the saccular macula destruction group and the stapedectomy group indicates that threshold alteration in the saccular destruction group is probably from the procedure of macular destruction however even after extensive saccular macula destruction the threshold change was far less than expected The group with saccular membrane rupture without macular destruction is currently under investigation and all details pertaining to this category will be reported in subsequent studies.

The data of the stapedectomy group in the present investigation could not be compared with the results after stapedectomies in humans. The present data was obtained from normal (with no disease process towards the inner ear) trained squirrel monkeys after simple stapedectomies which required minimal manipulation

ACKNOWLEDGMENT

Sincere appreciation is expressed to Mr R F Cruver and Mr S M Lansdon for their technical assistance

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LOCALIZATION OF SOUND DURING SIMULATED UNILATERAL CONDUCTIVE HEARING LOSS

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Thirteen *S* were required to localize pulsed noise in an acoustically treated room while th ir head movements were restricted. Judgment were mad (*a*) with both ears unoccluded nd (*b*) with the right ear occluded so that it input was ttenuated by 40 dB±5 dB. Performance wa highly accurate under both conditions and there were no significant differences betwee cond tions.

Systematic investigations of monaural localization have been relatively few and far between Most auditory localization studies have concentrated on apparent differences produced by a physical stimulus at the two ears (Mills, 1967) an approach based on the assumption that the difference cues are necessary and/or sufficient for explaining auditory localization. The occurrence of accurate localization with only one ear would contradict this assumption

Angell & Fite (1901) tested three *Ss*. One *S* had a unilateral hearing loss of some 26 years standing the other two presumably had normal hearing With head movements restrained, it was found that absolute accuracy of localization was worse for the monaural *S* than for either of the two binaural *Ss*, though practice did improve accuracy of judgments by the monaural *S* However the binaural *Ss* made many errors in judgment due to *front-back* ambiguities, while the monaural *S* did not

Ferree & Collins (1911) simulated unilateral hearing loss with an ear plug of unspecified composition. Their experimental *Ss* tended to displace apparent locale toward the side of the better ear but binaural *Ss* also showed a tendency to either right o left displacement

Jongkees & Groen (1946) used an earplug of paraffin and cotton to produce un lateral attenuation reducing sensitivity of the plugged ear by about 15 dB Localization in the vertical plane was apparently not affected

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Apparatus

The test stimulus was a pulse of 0 12 msec duration occurring repetitively every 105 msec It was presented through a 2 1/4 inc. Quam 22A06Z speaker mounted at the end of a movable boom 57 in. from S's head in the plane of his interaural axis. The center of rotation of the boom was perpendicular to and bisected S's interaural axis. The stimulus continued until S had made a final response

In order to minimize sound leakage into the occluded ear S blocked off his left ear with his finger while the plug was in place in his right ear The stimulus was then attenuated to the point where he reported he could not hear it. This stimulus intensity level was used for testing.

The boom was moved by a motor controlled from E s position in the test room. During its movement white noise was turned on for a fixed period of time to mask cues from duration of the noise of the boom motor

The S was seated blindfolded in an adjustable dental chair in a semi darkened, acoustically treated room. Head movement was restricted by tightening around his head a plastic band which was attached to the head est of the dental chair

Training and Testing

There were 16 test positions, each 22.5 apart at the level of S's ears. Immediately prior to tl e test session S was instructed as to the *names* of positions to be used. He was instructed only to close his eyes and press his head back against the backrest of the chair while making judgments. After each judgment, he was instructed to point to the source of the speaker then open his eyes. This feedback training was used for both listening conditions.

In the test situation each S made 5 judgments at each of 8 *positions* presented in random order without feedback The set of test positions was varied from condition to condition and from S to S so that each of the 16 positions was tested.

Audiometric and the two locale tests were administered in three separate sessions lasting from 1 / hours to 1 / hours each each S was tested under each condition (*a*) both ears unoccluded (Binaural) (*b*) right ear occluded (REO)

RESULTS

Fig. 1 is a composite audiogram for ne S showing each ear separately and the ffects of occlusion fo the ascending sweep of the audiometer

If S's tru threshold lies at or near the midpoint of line draw between a point on one hand t which he just did not hear tone and point on the other hand t hich he just heard tone w may then pl t probable threshold curv for him by connecting these midpoints. The curves shown here were derived in this manner from the original Békésy tracings

at all by this procedure horizontal plane localization particularly on the side of the unoccluded ear was considerably reduced Practice led to considerable improvement

Jongkees & van der Veer (1958 *b*) performed a direct test of monaural hearing and found that total monaural deafness did not preclude directional hearing Where there were no pinnae present head movements seemed to be mandatory for good localization

Bauer *et al* (1966) had *Ss* wear Vol R plastic earplugs for periods ranging from 6 hours to 6 days with testing at approximately 6 hour intervals. While *Ss* localized poorly at first continued exposure tended to improve performance Again displacement of apparent locale toward the side of the unobstructed ear was reported

Butler & Naunton (1967) used an MSA muff to occlude one ear and tested accuracy of localization as a function of stimulus intensity Their *Ss* were relatively accurate at higher sensation levels whereas stimuli tended to be displaced toward the unoccluded ear at the lower levels.

This latter report would tend to support the binaural intensity theory of directional hearing Once the mass of the ear obstruction has been overcome as at high intensity levels, then the effect of blocking the ear is minimized This might also explain the finding of Jongkees & van der Veer (1957) to the effect that conductive impaired patients had better directional hearing than sensorineural impaired patients which led them to propose that an intact cochlea is a primary requirement for good localization.

In general these experimenters agree that reasonably good localization is possible with only one ear provided complex sounds are used Jongkees & Groen (1946) using a variety of test stimuli found that monaural localization was especially poor for pure tones. However the same was true of *Ss* with binaural hearing The ability to localize pure tones is not necessarily relevant to an understanding of localization in general since there are few non-experimental situations that require localization to pure tones

To the extent that binaural differences operate as has been proposed (Mills, 1967) their systematic disruption should lead to systematic changes in locale determination The present experiment was designed to compare the effectiveness of monaural and binaural localization in the same *Ss* thereby testing the validity of binaural difference theories of auditory localization

PROCEDURE

Audiograms were made for each unoccluded ear for each of 13 *Ss* using a Grason Stadler Békésy-type Audiometer Model E800 Earplugs of Silastic RTV Silicone Rubber Compound and cotton batting were made so as to fill all the convolutions of the pinna and to cover the backs of the pinnae of *Ss* right ears. Finally audiograms were made for the occluded ear

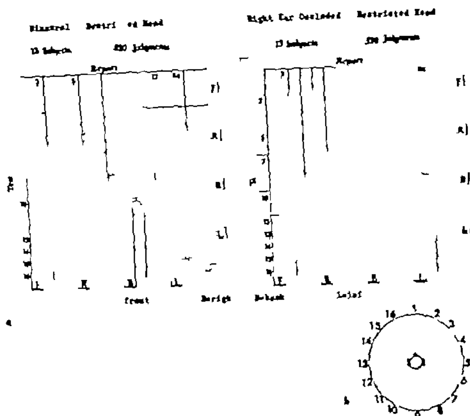


FIG. 2. Scattergram showing relationship between Test Positions and Report Positions. (a) Binaural condition—both ears unoccluded; (b) REO condition—right ear occluded.

tion 1 errors could be made only *rearward*, while from Position 9 errors could be made only *forward*. Thus, *Position 1* produces no positive errors, and Position 9 no negative errors.

The Binaural and REO conditions *did not differ significantly* as to direction of errors or *percentage of errors in either direction*. Also, there were no significant differences measured *either* within or between experimental conditions as to right and *left sided errors*.

Correlation between mean error scores and IAD was .089 for REO and .0081 for the normal hearing condition. This finding is in agreement with Hochberg's (1963) report that IAD scores are not predictive of localizing performance.

DISCUSSION

These *S*s were highly accurate in auditory localization judgment under either condition and there was no significant difference in accuracy between

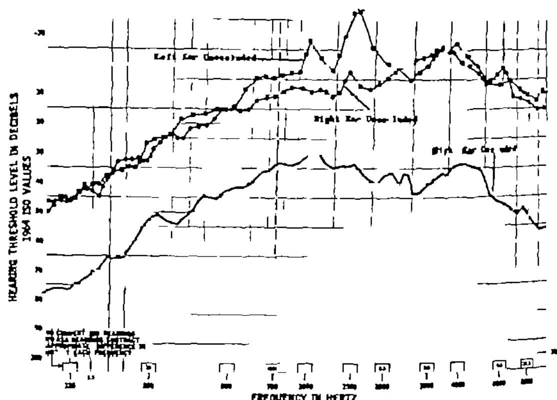


Fig 1 Threshold curves fo on S showing ffect of occlusion in ne ear

All threshold measurements for this *S* with unoccluded ears, were well within normal limits However the left ear did test slightly more sensitive than the right ear

With REO sensitivity for pure tones was reduced on the average by 40 dB $\pm$ 5 dB Hochberg (1963) had reported that for complex signals, 22 dB or greater Interaural Audiometric Differences (IAD) affected localization.

Figs. 2 *a* and 2 *b* are scattergrams showing the relationships between true or Test Positions of the stimulus and Report Positions. Each point represents one judgement by One S Both experimental conditions produced very high correlations between report positions and test positions in the Binaural condition 0 91 and in the REO condition 0 89 ($p < 0.01$ in both cases, Pearson Product Moment Correlation)

All responses were considered for error analysis. The number of test positions of deviation was taken as the measure of size of error For the group as a whole, the differences between the size of the errors under the two conditions was not significant (*A* test Sandler 1955)

Because of the apparent tendency of *Ss* to refer stimulus positions rearward we compared rearward errors with forward errors Fig 3 shows the mean size and direction of errors at each test position For scoring errors rearward deviations were given a negative sign forward deviations a positive sign

Positions 1 and 9 must be considered as special cases, since from Posi

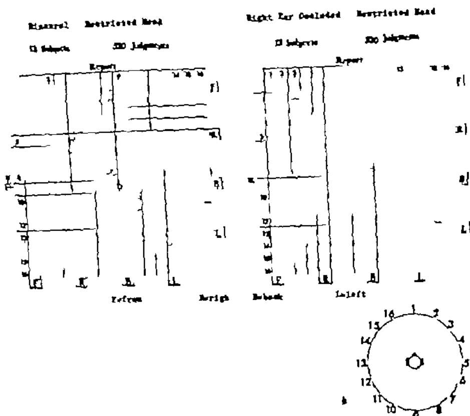


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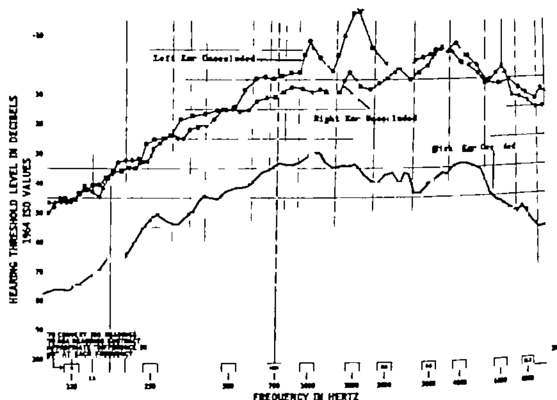


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condition as in the REO condition (16 to 5) Angell & Fite (1901) made a similar observation

Nordlund (1962 *a*, 1962 *b* 1963) has investigated the physical factors in angular localization at some length He concludes that interaural intensity differences are unreliable indicators of azimuth at higher frequencies and that interaural time differences are inadequate, e.g to distinguish front from back, and suggests that head movements are necessary to resolve such problems although he has not tested this directly

If binaural cues are neither necessary nor sufficient for accurate localization under all conditions, then we are forced to postulate additional mechanisms.

Wallach (1940) has made a case for the proposition that small head movements are combined with binaural differences to provide adequate cues for auditory localization However reaction times are of the order of 100–200 msec. (Woodworth & Schlosberg, 1954) while many of the sounds to which we are obliged to attend are of shorter duration, and do not occur one at a time as in the controlled, quiet atmosphere of the laboratory

Jongkees & van der Veer (1958) have proposed that small movements of the head may assist localization in the absence of pinnae. But, based on physical measurements of the filtering effect of the pinnae they felt that these structures played an important role in determining direction, particularly in elevation, for complex sounds with strong features above 5000 Hz.

The hypothesis that the pinna plays a significant role in auditory localization is compelling and perhaps necessary if we view the entire mechanism of hearing as a kind of broadband receiver with fine tuning capabilities Interaural differences of time and intensity would then provide a facility for selecting that ear to which we might wish to pay attention Having decided on this, we could then turn our heads, provided the situation was appropriate to maximize the informational input to that ear and to select it, and squelch those other signals in the environment to which we did not wish to pay attention. Under these circumstances, it becomes mandatory that we allow of a structure that provides localization information to a first approximation.

Batteau (1967 in press) has measured delay paths related to the structure of a single pinna which can be mapped on the coordinate system for locale 0–80 microsec for azimuth and 100–300 microsec fo elevation. He suggests that the pinna serves as a mechanism for auditory localization so that one ear would be sufficient and head movements would not be essential

Fisher & Freedman (1967) have tested the feasibility of the pinna hypothesis and found that, under conditions of restricted head movement pinnae must be present for accurate localization

While the present experiment did not directly test the pinna hypothesis, the accuracy f locale determinati n measured with one ear occluded forces n t postulate some such alt rnate system th t could operate in the absence of binaural cues.

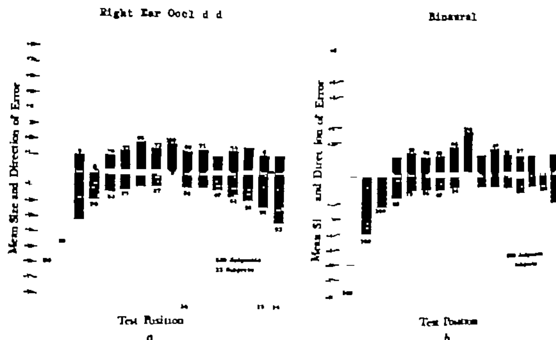


FIG. 3 Mean si e and direction of error at each test positi n. (*a*) Binaural condition (*b*) REO condition The numbers at the ends of the bars indicate the percentage of error in either directi n

the two conditions These findings confirm the reports of other investigators (Angell & Fite, 1901 Ferree & Collins 1911 Bauer *et al.*, 1966 Butler & Naunton 1967) that accurate monaural localization is possible

Contrary to the findings of other investigators (Ferree & Collins, 1911 Bauer *et al* 1966 Butler & Naunton 1967) our *Ss* manifested no con sistent or *significant shifts toward the side of the unoccluded ear that* were not also evident when neither ear was occluded In fact the only com parison for size and direction of error that was significant in the REO con- dition was that larger rearward errors were measured on the side of the unoccluded ear This may be considered a shift away from the more sensitive ear

Due to the fact that we have two ears one on either side of the head, the study of auditory localization has tended to concentrate on interaural differences (Mills, 1967) Such concentration assumes that interaural dif ference cues are essential to accurate localization Our findings are quite at odds with this assumption Interaural difference cues appear to be suf ficient for accurate localization under certain conditions (e g., when head movement is permitted) but are hardly necessary under all conditions as this study has shown

It is not difficult to specify conditions under which binaural difference cues are insufficient for accurate localization For example when head movement is restricted there are more front–back difficulties with two ears than with one ear In the present experiment the front position was in correctly reported as the rear position three times as often in the Binaural

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VESTIBULAR HABITUATION IN BALLET DANCERS

P. OSTERHAMMEL, K. TERKILDSEN and K. ZILSTORFF

From the University E.N.T. Clinic, Rigshospitalet, Copenhagen, Denmark

Thirteen ballet dancers and 9 normal subjects were examined by means of high velocity rotation and electronystagmographic recording of the postrotatory response. According to accepted definition the ballet dancers showed a significant degree of habituation. The so called spotting technique caused a definite reduction of the postrotatory reaction. Dancers with intense nystagmus reactions were even as immune to vertigo as those with slight nystagmus. In some of the subjects the nystagmus tended to perpetuate for long periods no matter how it was elicited thus also after optokinetic stimulation. The vestibulo-ocular response following rotation is influenced by so many factors that it becomes a very unreliable measure for balancing proficiency in dancers.

Vestibular habituation can readily be induced in experimental animals by repetitive application of identical stimuli, and there will be a gradual response decline.

Investigations on human subjects have not yielded the same uniform results. Of special interest in this respect is the behaviour of individuals belonging to professional groups, where the daily routine involves exposure to extreme degrees of stimulation.

Thus Collins (1966) submitted 9 professional figure skaters to a number of vestibular tests including also on-ice performances. Eye movements were recorded by electronystagmography (ENG) and the use of telemetering technique permitted recording also during the free performances. Contrary to previous investigators (Mowrer 1934, McCabe, 1960) he found vigorous postrotatory nystagmus and suggested that the absence of opportunities for visual fixation might explain this discrepancy. He concluded that possibly nystagmus responses of skaters in total darkness may differ in some way, on the average, from responses of ordinary subjects, but a larger sample of skaters, quantification of nystagmus and statistical comparison with a non-skater group would be required to establish this relation.

There are no similar investigations with regard to ballet dancers. In the old literature it is often mentioned as a well known fact, that practiced dancers are immune to vertigo, and there are several reports about the ab-

This work was supported by grants from the P. A. Brandt Foundation.

ZUSAMMENFASSUNG

Dreizehn Versuchspersonen lokalisierten pulsierende Laute in einem akustisch behandelten Zimmer währenddessen Kopfbewegungsfähigkeit eingeschränkt war Die Lautrichtungen wurden unter zwei Bedingungen lokalisiert a) mit beiden Ohren frei und b) mit dem rechten Ohr so verschlossen dass die Hörfähigkeit auf 40 dB±5 dB vermindert war Die Leistungsfähigkeit war sehr genau unter beiden Bedingungen und es wurden keine statistisch signifikanten Unterschiede zwischen den Bedingungen gefunden

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the person who operated the chair to drive it at a higher speed In the final evaluation we thought it permissible to consider the stimuli as being identical, and that the effect of slightly shorter duration employed in the dancers would be outweighed by the higher velocity Interpolation from the curve for averaged normal responses seems to indicate that the fault committed by such an approximation is negligible

We examined a total of 13 dancers, 6 males and 7 females. The average age was 27 years, with a range from 18–35 years Seven were first dancers and 6 were ordinary members of the corps. The examination was conducted at the very end of a busy ballet season, where they were in top physical training Two were re-examined at other periods. One of these cooperated very kindly in preliminary testing through which the standard procedure was laid down

They were all submitted to the following test schedule Calibration. Ten rotations with closed eyes first in the clockwise (cw) and then in the counter-clockwise direction (ccw) As in the normal series they were carefully instructed to keep the eyes in a midline position during the recording period. The session was immediately continued with 10 cw and 10 ccw rotations, during which they employed spotting technique. Instructions were to close the eves as soon as the chair came to a complete stop and to attempt keeping the eyes in a midline position during the recording Is was a rare experience to examine such a group of highly motivated subjects and they all perf rmed carefully according to instructions

RESULTS

The plan called for registration of the subjective responses after each 10 rotations. This became a monotonous affair A minority reported some slight feeling of unsteadiness during the first few seconds after the first rotation period, but therwise no one would *testify to any feeling of* dizziness. Their position in the chair was relaxed, which was in strict contrast to our experience with the normal group, where after such strong stimuli most of the subjects would actually cling to the armrest in their effort t maintain balance One dancer demonstrated how she was able to walk straight f rwards, with closed eves, heels to toes, immediately after pirouetting during a period of 10 sec Ballet shoes have very narrow soles, which adds considerably to the difficulty of this particular performance

Table 1 gives a comparison between nystagmus responses in normals and in ballet dancers when rotations are performed with *closed eves. In spite* of th relati ely small number of test subjects in both groups the difference i significant f r all the recorded periods.

The figures in Table 2 give the response in *ballet dancers with and* without the use of spotting. *The difference is highly significant for all* parameters and the figures are strong *objective evidence for the advantage* f using spotting during *pirouetting.*

sence of postrotatory nystagmus when eye movements are observed visually (Mowrer 1934 Tschiassny 1957)

Having had the opportunity to examine a group of highly proficient dancers from the Royal Danish Ballet we decided beforehand to establish a standardized procedure which permitted quantification of the results, and to undertake a comparison with a normal material of naïve subjects (Osterhammel *et al*)

All modern ballet dancers employ the so called spotting technique Before starting a pirouette they select some easily identifiable object which is kept in focus during the entire turn as a point of reference. While the body rotates in the initial part of the pirouette the head remains almost immobile With about one half of the rotation completed the head is turned in a very quick motion covering an arc of about 180 in order to regain view of the spotting object Ballet dancers consider this spotting as very important for maintaining balance and they devote much energy to learning the correct execution of the movement. This particular technique eliminates the possibility of undertaking an ideal comparison with normals, and it became necessary to examine the dancers both with and without the employment of spotting In this way we became able also to evaluate the influence of spotting on the vestibular response

OWN INVESTIGATIONS

Our previous report gives a detailed description of the methodology We employed a Barany rotating chair which was operated manually at velocities of around 280 /sec Maximum velocity was attained at the beginning of the second turn and deceleration to complete stop within one half turn. Eye movements were followed by means of ENG After amplification of the signal it was transferred to the recorder by F M telemetry technique. The normals were submitted systematically to a succession of unilateral rotations according to the following schedule 3 6 9 12 9 6 and 3 rotations. Of various means for scoring the results the slow phase eye displacement immediately after the rotation gave the best correlation between stimulus and response Velocity of slow phase eye displacement in deg/sec was evaluated for the periods 0–10 sec 10–20 sec and 0–20 sec where 0 indicates the end point of rotation With 9 rotations the response was intense and tended to approach a maximum and it was decided to use a stimulus of this magnitude during the examination of the dancers. For unknown reasons the chair came to be rotated somewhat faster in the session with the dancers While the normals were submitted to 9 rotations during an average period of 12 6 sec the dancers were rotated 10 times during an average period of only 10 sec with variations from 8.8 to 11.2 sec The explanation is partly to be sought in lighter physical weight of the dancers. Possibly also the vivid spotting movements may unknowingly have induced

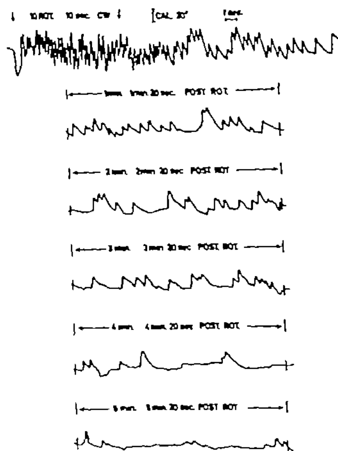


FIG. 1. Recording from dancer showing very strong postrotatory response. Nystagmus persist almost indefinitely.

parison with the results obtained in the sober condition, showed an increase of low phase eye velocity from 36 /sec to 56 /sec without spotting, and from 16 /sec to 37 /sec with spotting.

DISCUSSION

Our results show without any reservations that the vestibuloocular response in ballet dancers, on the average is smaller than in normals when they are exposed to high velocity rotation.

The possibility should be considered that this difference might be explained by some kind of selection. This possibility was definitely refuted by the dancers themselves. Dancing on tiptoes, and thus the training with pirouettes, is omitted during the early school years in order to avoid permanent damage to the immature foot through this unnatural strain. If candidates leave school it is not because of problems with balance, and we

TABLE 1 *Nystagmus responses in normals and ballet dancers without the use of spotting technique*

Rotation	Post. rot. period (sec)	Mean values, slow phase velocity (/sec)		Levels of significance (P)	
		Normals	Dancers	0.05	0.01
CW	0–10	46	37	+	
	10–20	29	20		+
	0–20	38	28		+

A comparison between the average cw and ccw values for first dancers and ordinary corps members gave a P value of 0 05 which is significant at the 5 pct level

From a professional viewpoint 5 dancers were considered to have a better than average balance. A comparison of the results from these 5 with the remainder of the group showed no significant difference (P 0 1–0 05)

Five were older than 27 years and 8 were younger The P value for these two groups was also between 0 1 and 0 05 showing no significance The results for males and females were almost identical

In routine training turns are performed both cw and ccw During actual performances, however pirouettes are mostly executed in the cw direction Both with and without spotting the average results for these two directions were suprisingly similar for all parameters

One male dancer was re-examined after two hours during which he enjoyed 9 strong drinks Subjectively he felt somewhat intoxicated, but he was completely balanced and without spontaneous nystagmus. A com-

TABLE 2 *Nystagmus responses in dancers with and without spotting technique*

Rotation	Post. rot. period (sec)	Mean values, slow-phase velocity (/sec)		Levels of significance (P)	
		With spotting	No spotting	0 01	0.001
CW	0–10	29	37	+	
	10–20	16	20		+
	0–20	23	28	+	
CCW	0–10	29	39	+	
	10–20	17	22		+
	0–20	23	31		+

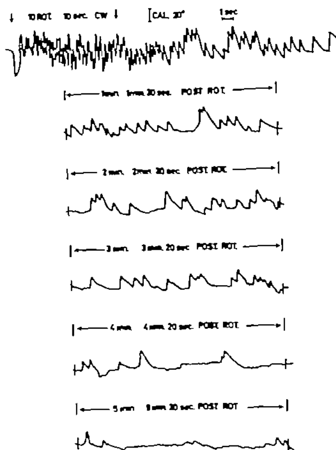


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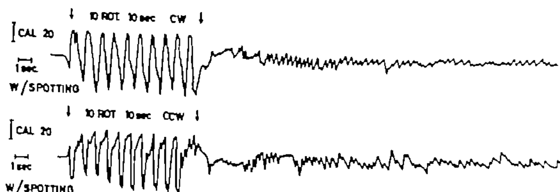


Fig. 2 Recording from dancer employing spotting technique The appearance of strong typical nystagmus beats is delayed for about 4 sec after complete stop of the chair

were told axiomatically that anybody can be taught a sufficient degree of balancing Thus, according to accepted definitions it can be stated that the vestibulo-ocular reflexes in ballet dancers are subject to habituation, and also that on the average, it is most pronounced in dancers with the highest experience A number of observations, however deserve special mentioning, and tend to modify our statement so far that it becomes almost meaningless

Some of the dancers exhibited very strong nystagmus (Fig 1) Nevertheless they appeared to have the same degree of immunity to vertigo as the rest of the group and their general reaction to rotation was completely different from normals with approximately the same degree of nystagmus.

Mowrer (1935) published a series of observations in pigeons, which like other birds react with nystagmus of the entire head and proved that several factors tend to prevent the occurrence of postrotational vestibular nystagmus when vision is permitted during the rotation It was evident that the rythmic movements of the head during the rotation stimulate the vestibular receptors in such a manner as to lessen the vestibular effect produced by the retardation of the subject In many ways head nystagmus is similar to the spotting of ballet dancers, and our findings show that these movements just as effectively cause a reduction of the postrotational vestibular response in humans

Furthermore Mowrer observed a tendency of the rotational nystagmus to persist at the end of the period of rotation At this point the persisting visual and the induced vestibular nystagmus are in opposite directions, and there will be a struggle for dominance of the final common path" Three of the dancers showed consistently a standstill of the eyes during the first 4–5 secs (Fig 2) immediately following those rotation tests, where spotting technique was employed. We interpret this as evidence of the same struggle for dominance of opposing nystagmus tendencies. Subjectively the dancers were not aware of phenomena referable to such mechanisms, but according to Mowrers observations (1937) they may have contributed to the smaller response obtained after rotations with

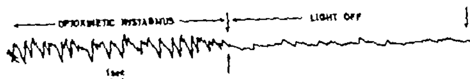


Fig. 1. Recording from normal person. The optokinetically induced nystagmus persist after end of stimulation period.

spotting. A striking demonstration of the tendency for nystagmus to persist when first elicited was seen in several dancers. In one the nystagmus would continue almost indefinitely as slow movements with a large amplitude and in the same direction as the initial brisk nystagmus (Fig. 1). This dancer was re-examined at a later period and with exactly the *same* result. It should be noted that she experienced no discomfort following the tests and could not testify to any subjective postrotational vertigo.

There is no mention in modern vestibular literature about these post stimulus *persistence tendencies* of nystagmus, or how they may influence various response *parameters*. They can be *demonstrated in pure form* following optokinetic nystagmus.

Fig. 3 shows an electronystagmographic recording following a period of optokinetic stimulation by means of rotating light spots in an otherwise *completely* dark room. At the arrow the light was turned off and the person would attempt to keep her eyes in a midline position. The room was completely dark and there was no possibility for fixation even with the eyes open. The moving spots were not so bright that they left any optical afterimage.

In conclusion it can be stated that the electronystagmographic response to vestibular stimulation appears *to* be influenced to a very considerable degree by mechanisms about which we know very little. One factor is a tendency for nystagmus to perpetuate by itself after the termination of *any* specific eliciting sensory activity. *Habituation* of the response is another factor. In one male dancer a moderate degree of alcohol intoxication caused dishabituation. We agree with Aschan (1967) that this points to a central origin of professionally induced habituation. The influence of *these and* probably other factors on the vestibulo-ocular response is erratic and the correlation to the kind of habituation, which enables a person to *perform* adequately following intense vestibular stimulation is ambiguous. The fact that statistical comparisons show smaller responses in ballet dancers on the average, should not lead anyone to take the outcome of such tests as a measure for the individual dancers proficiency in maintaining balance.

ACKNOWLEDGMENT

Grateful acknowledgment is made of the cooperation and interest rendered by The Royal Danish Ballet, Copenhagen.

ZUSAMMENFASSUNG

Dreizehn Ballettänzer und neun Versuchspersonen wurden elektronystagmographisch nach sehr schneller Rotation untersucht, um die postrotatorische Reaktion zu messen Bei allen Ballettänzern wurde eine signifikante Habituation gefunden und die sogenannte „spotting technique" verursachte eine signifikante Reduktion der postrotatorischen Reaktion Ballettänzer mit starker Nystagmusreaktion waren ebenso immun gegenüber Schwindelgefühl als jene mit nur geringer Nystagmusreaktion Bei einigen der Ballettänzer und einigen der anderen dauerte der Nystagmus längere Zeit an unabhängig davon auf welche Weise der Nystagmus hervorgerufen war also auch nach optokinetischer Stimulation Die vestibulo-okulare Reaktion nach Rotation hängt von so vielen Faktoren ab, dass es nicht möglich ist sie als eine zuverlässige Methode zur Messung des Gleichgewichtes bei Ballettänzern zu betrachten

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BÉKÉSY AUDIOMETRY AND CLINICAL MASKING

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Békésy audiometry was performed in 31 patients with unilateral perceptive hearing loss, both in quiet and with 80 dB masking of the unaffected ear. The test tones and masking noise were applied with insert type receivers. The masking noise was found to increase the separation between "I" and "C" tracings, as well as to cause a highly significant reduction in the tracing amplitude of fixed frequency "C" tracings at 250 and 1000 cps, and of sweep-frequency "C" tracings at both lower and higher frequencies. In 7 patients, the masking changed an audiogram of Jerger type I to type II; in 7 patients it changed an audiogram of type II to type IV, and in 3 patients it changed type I to type IV. The relation between the tracing amplitude for "I" and "C" was also changed. It is concluded that no matter what the parameter used in the evaluation, the result is often decisively influenced by the masking delivered to the non-test ear.

In our preliminary communication (Blegvad & Terkildsen, 1966) we reported the observation that in patients with one-sided perceptive deafness, marked changes were found in the Békésy audiogram on exposure of the non-test ear to masking noise. The changes consist of a separation between the curves recorded with an interrupted ("I") and a continuous tone ("C") and a reduction in the tracing amplitude in the latter curves. The aim of the present study was to provide a quantitative evaluation of those changes in the Békésy tracings, resulting from masking of the unaffected ear.

METHOD AND MATERIAL

As in the above-mentioned study a Grason-Stadler E-800 audiometer was used, the TDH-39 telephones of which were replaced by two Beyer DT 507 insert-type receivers. The characteristics of these have been described previously (Blegvad & Terkildsen 1967). In comparison with the TDH-39 telephones, they have a somewhat higher sensitivity at low frequencies and somewhat lower sensitivity at high frequencies. As the sole aim of the study was to note the relative changes in the audiogram resulting from the masking noise we found no grounds for adjusting the compensat

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ing cam of the audiometer to the frequency response curve of the insert telephone The white noise generator of the audiometer was used for masking Whatever the hearing threshold of the better ear a noise intensity was used with an overall SPL of 80 dB (measured in a 2 cc coupler) This is the masking level we usually employ with Békésy audiometry in patients suffering from a moderately pronounced unilateral perceptive hearing loss. Two or three practice runs were made in which the unaffected ear was employed and then the actual Békésy investigation was made limited to the affected ear

The following curves were recorded (1) sweep-frequency tracings for I" and "C (2) fixed frequency tracings at 250 1000 and 4000 cps for both "I and C for periods of 2 minutes and 15 seconds each The aim was to start the tone from a subliminal level and the first 15 seconds of the tracing were not included in the subsequent analysis of the results. The rate of attenuation was always the slower of the two standard possibilities (125 dB/min) All determinations were made both without and with masking In the tracings made without masking the insert telephone was removed from the unaffected ear and the ear was covered with a circumaural noise defender in which—in order to reduce the occlusion effect—we had increased the size of the cavity The sequence of testing the various conditions was varied with the exception that corresponding I and "C" tracings were always recorded in that order It should be mentioned that the procedure differed somewhat from that followed in the preliminary studies, where fixed frequency tracings were recorded with gradually increasing masking This had made it possible to observe the effect of different masking intensities within a relatively brief period of time and it had been observed that in some cases as weak a masking as 50–60 dB had been sufficient to elicit excessive changes in threshold in patients with a retro-cochlear lesion The procedure used in the present study has the advantage that it permits to a higher degree a numerical evaluation of the influence of masking on the various curve parameters, for example the tracing amplitude

The investigation comprises 31 patients, suffering from predominantly unilateral perceptive hearing loss Their ages varied from 23–78 years (mean 51 years) The hearing impairment in the affected ear (average for the speech frequencies) was within the limits of 25–70 dB[1] The audiometric pattern could roughly be classified as follows (according to Johnson & House 1964) Flat loss 14 low frequency 7 high frequency 9 trough shape 1 In a number of the patients the hearing in the unaffected ear was somewhat reduced, in particular an impairment in hearing at the high frequencies was quite frequently present In selecting the patients, special care was taken that the difference in the acoustic function on the two sides was such that in the examination without masking crosshearing could

[1] re ISO 1964 standard.

be excluded with reasonable certainty In some cases, patients were deliberately selected in whom there was a certain degree of perceptive hearing impairment in the non-affected ear as this made it possible to include patients in the material with rather over moderately severe loss of hearing. With respect to the clinical diagnosis, the patients were distributed as follows Menière's disease 20 Sensorineural Unknown 7 Sudden Onset of Loss 3, Acute Noise Trauma 1 The diagnoses indicated were made by the staff of the Department of Otolaryngology University Hospital Copenhagen, in many cases in collaboration with the staff of the radiological the neurological, the neurosurgical and the ophthalmological department The diagnosis Menière's disease presupposed the symptom triad hearing impairment, tinnitus and vertigo while it was not considered a *necessary* criterion that the hearing should be or should have been fluctuating, or that the vertigo should occur in acute attacks. In none of the patients did the neuro-otological examinations give evidence of a tumor in the cerebellopontine angle

RESULTS

Audiograms recorded without and with masking were compared and the material was analysed with respect to (1) thresholds, (2) separation between corresponding I and "C" tracings, (3) tracing amplitude (4) audiogram types (classified according to Jerger 1960)

1 *Thresholds*

The influence of ma king on the threshold values was determined from f xed-frequency tracings, the threshold being determined with the aid of a visually interpolated mid-line between the tops and the bottoms of the excursions. In most patients, the thresholds for both "I" and "C" were stable after the course of 1 minute, and showed only such variations as could be ascribed to th slow oscillations already described by Békésy (1947) In such cases, we employed the mean threshold for the 2nd minute In a few patients, in whom the threshold during the 2nd minute still did not appear stable i.e. where the thresh ld change had the same direction throughout the whole period of 2 minutes, the threshold used was that obtained fr m the last 15 seconds of the tracing

Fig 1 hows the mean differences between the threshold values determined with masking and without masking The absolute values should be accepted with a certain reservation, as a greater or lesser degree of perfect adaption of the insert-telephone to the external meatus implies some uncertainty in the determination, particularly at the low frequencies. It is evident, however that the threshold changes caused by the masking are on the average greater for "C" th n for "I" In our study of contralateral masking and Békésy udiometry in normal listeners (Blegvad 1967) we found greater threshold shifts for C" than for "I" but only at 1000 and 4000 cps.

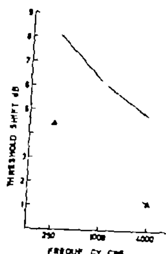


Fig 1 Mean threshold shifts produced by contralateral masking as a function of test tone frequency Results from 31 patients with (predominantly) unilateral perceptive deafness examined in quiet and with 80 dB SPL wide-band masking of the better ear Tone presentation Δ Δ, Periodically interrupted ("I"); ●——● continuous ("C")

2 Separation

Just as in normal listeners the masking effect varied in the individual patient In some, the masking did not result in any definite change of threshold while in others the thresholds for "I" and "C" were changed almost equally while in others again the change for "C" was considerably greater than the change for "I" and in the individual patient changes varied with frequency In the examination without masking the threshold for "I" was often better than the threshold for "C" In view of the above findings, therefore a comparison was made between the threshold for "I" and the threshold for "C" in the same individual in other words the separation between the mid points of corresponding "I" and "C" tracings, both with and without contralateral masking Table 1 shows the overall results for the 31 patients At all 3 frequencies the separation is somewhat greater in the masked condition than in the unmasked condition Also in sweep-frequency curves, masking resulted in an increased separation between the "I" and "C" tracings As it is a more difficult task to trace the threshold in the case of a tone of constantly changing frequency than it is to trace a threshold in the case of a tone of constant frequency we considered the fixed frequency curves as more suitable for the numerical evaluation

3 Tracing amplitude

The number of pen swings per minute was determined on "I" and "C" fixed frequency tracings for the 1st and 2nd minute separately and the mean amplitude in dB was calculated from this in the usual way The results are shown in Table 2 together with the mean value for the whole period of 2 minutes The table also shows the mean tracing amplitude for "I" and "C" sweep-frequency tracings for the 250 to 1000 cps range and

TABLE 1 *Separation (dB) between corresponding I" and C" fixed-fre quency tracings in quiet and with contralateral masking*

Positi ntries ignify that I" tracings were traced t lower sound pressure lev l the "C" tracings.

Masking level (dB)	250 cps			1000 cps			4000 cps		
	Mean	Median	Range	Mean	Median	Range	Mean	Median	Range
0	4 6	4 0	−3.0 to 10 0	5.9	6.0	−3.0 t 15 0	9 4	9.8	2.0 t 21.0
80	7 4	7 0	0 t 22.5	8.2	8.5	0 to 20.0	12.5	11.8	1.5 t 30.0

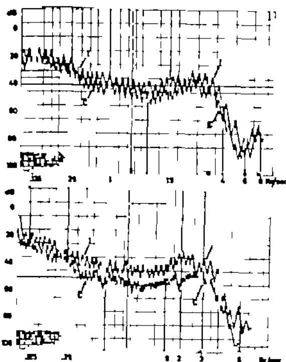
the 1000 to 4000 cps range The amplitude was calculated in the same way as for fixed f equency tracings (determination of the number of pen swings per unit time and conversion of this value to dB) The tracing amplitude without and with masking was compared in the individual patient, and the average difference for the material as a whole was examined with Student s *t*-test to determine whether it was significantly different from zero. The result of the statistical analysis is given in the table by the asterisks. As stated, in fixed-frequency "C" tracings, masking resulted in

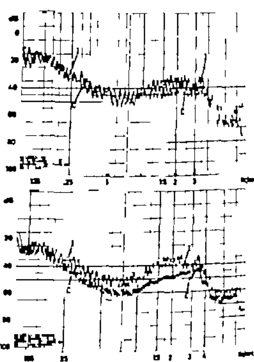
TABLE 2 *Mean tracing amplitude (dB) in quiet and with contralateral masking*

Asterisks indicate that the changes produced by masking were found t be significant (a d for $P<5$ 1% and 0.1% respectiv ly)

Masking level (dB)	250 cps			1000 cps			4000 cps		
	1st min	2nd min	Average	1st min	2nd min	Average	1st min	2nd min	Average
Fixed frequency I" tracings									
0	8 12	8.13	8.12	7 77	7.62	7.69	7 47	7.59	7.52
80	.29	7 70	7.61	6.91	7.28	7 10	6.65	6.96	6.80
Change	0.83	0.43	0.62	0.86**	−0.34	0 59*	−0 83	−0 63	−0.72
Fixed frequency C" tracings									
0	7.37	7.23	7.40	6.28	5.91	6 10	4.74	4.22	4 47
80	5 67	5 69	5.78	4 62	4 43	4.52	3.90	3.92	3.93
Change	1 70**	−1.31	1.62**	1.65	1.53	−1.58	−0 73	−0.31	−0 51

Masking level (dB)	Sweep-frequency I" tracings		Sweep-frequency "C" tracings	
	250–1000 cps	1000–4000 cps	250–1000 cps	1000–4000 cps
0	8.71	8 83	7.60	6.37
80	8.46	8 68	5 43	4.46
Change	−0 24	0.17	2.17	−1.93*


Fig. 2.


Fig. 3.

Figs. 2 to 9 Example of sweep-frequency tracings obtained in quiet (upper part of figures) and with 80 dB SPL contralat al masking (l wer part of figures) +20 dB in the legend be e th a figure indic te that th int nsity of the test t es had been increased 20 dB abo the st ndard l v l by use of the ±20 dB control witch of the audiom t (thu making th h aring l ss appe r less than its actual size)

Fig 2. Tracing in a 66-yea -old f mal with left M nière s disease +20 dB

Fig 3 Tracing in a 45-yea -old male with right Menière disease +20 dB.

a highly significant reduction in the tracing amplitude at 250 and 1000 cps, and in the sweep-frequency C" curves, the reduction was found to be highly significant both for the lower and the higher frequency ranges. The reduction was less pronounced in the fixed frequency "I" tracing and the amplitude did not change significantly in the sweep-frequency "I" tracings.

4 *Types of audiogram*

The audiograms were classified into Jerger s 4 types on the basis of an overall evaluation of sweep- and fixed frequency tracings. As mentioned by other authors (Johnson & House 1964 Owens, 1964 Hopkinson, 1966) it can sometimes be difficult to carry out a precise grouping Differentiation between type II and type IV in particular can give rise to discussion Johnson & House (1964) state that in type IV the gap between I" and "C" should be greater than 20 dB In one of the most recent otological handbooks Greiner & Conraux (1966) state that the gap is approximately 20 dB Jerger (1960) however in his original description of the four types, did not lay down any quantitative criterion He merely commented as follows

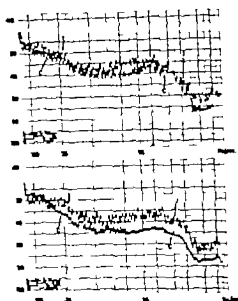


Fig. 4.

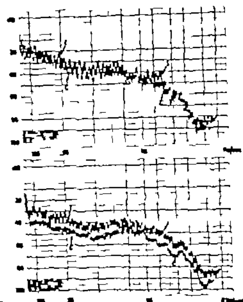


Fig. 5.

Fig. 4. Tracings I 37-year-old femal with left Menière disease +20 dB.

Fig. 5. Tracings in 61-y ar-old male with left side hearing loss resulting from previous ttacks f Menière's disease

Type IV tracings more closely resemble type II than type III but differ in one important respect. Th continuous tracing falls consistently below th interrupted t frequencies below 500 cps. At higher frequencies the continuous may fall a constant distance below the interrupted, resembling a *type II* in this respect. The tra ng width may or may t become abn rmally small, further adding to possible conf sion with type II. At mid- and high frequencies there may even be som erlap between C d I. The distinguishing feature however occurring in both con tional and fixed-frequen y tracings is th gap between C and I t relati ly low frequencies (100 to 500 cps)

In a subsequent description, Jerger (1962) comments s follows on sweep-frequency tr cings

I the type IV audiogram th "C" tra ing runs well below the I traci g at all frequenc es but seld m hows the precipitous drop f the type III. The type IV audiogram differs from th type II that there is not the overlap at low freque ies haracter stic f the type II. Also, th difference between C" and "I" much greater in th IV than in th II

With regard t type II he comments

I the type II audiogram th "C" tracing verlaps the I" tra ing at low frequen ies. Somewh re between 500 d 1000 cps, however it drops 10 t 15 dB below the I traci g d run below it but parallel t it ll th way out to th high frequency d.

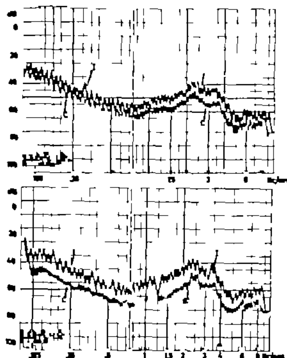


Fig. 6

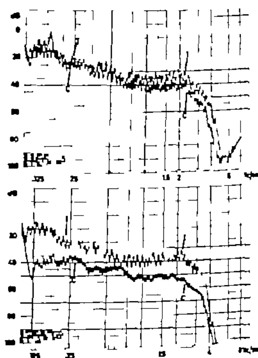


Fig. 7

FIG. 6 Tracing in a 47 year-old male with right Menière disease

FIG. 7 Tracings in a 67 year-old male with left sensorineural loss, cause unknown. + 20 dB

Compared with the characteristic of type II the characteristic of type IV possibly invites the comment that a gap of more than 20 dB should be present between I" and C in order that the audiogram can be labelled as type IV In this later description for that matter nothing is mentioned as to fixed frequency studies. In the illustration of a typical example of type IV by Myers *et al* (1962) the gap is clearly less than 20 dB at all frequencies

In Figs 2 to 9 some typical examples are shown of the influence of masking on the sweep frequency curves. We have kept to Jerger's original description and therefore consider it correct to classify audiograms such as those seen lowest in Figs 5 and 6 as type IV The audiograms shown lowest in Fig 8 and Fig 9 are incontrovertibly type IV Since grouping into types is by visual comparison between the course of the "I" and the "C" tracings, both the above described changes in the distance between the mid points of the curves and the changes described in the tracing amplitude are of significance for the result Without masking, 15 patients had an audiogram of type I 14 had an audiogram of type II and only 2 patients had an audiogram of type IV When the contralateral ear was masked only 5 patients had an audiogram of type I 14 had type II and 12 had type IV Type III did not occur In 7 cases, masking changed a type I audio-

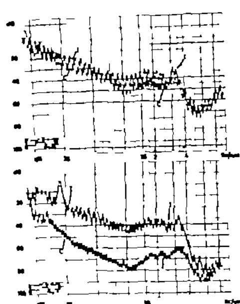


Fig. 8.

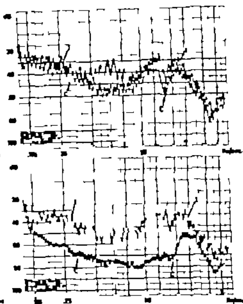


Fig. 9

Fig. 8. Tracings in 44-year-old female with left sensorineural loss, presumably Menière disease +20 dB

Fig. 9 Tracings in 54-year-old male with right sensorineural loss, cause unknown.

gram to a type II, in 7 cases a type II to a type IV and in 3 cases a type I to type IV The audiogram type was thus changed in about half of the cases examined

COMMENTS

Since Békésy described his self recording audiometer in 1947 this type f instrument has been increasingly employed in the audiological clinic. One f the chief fields of application of the Békésy audiometer is and has lways been differential diagnosis in cochlear and retro-cochlear lesions, fact which is f the greatest ctuality in patient with unilateral perceptive hearing loss. There have been numerous studies on the value of Békésy audi metry a a diagnostic tool. Many investigators have made measurement f the tracing amplitude on sweep-frequency curves (in Scandinavia mainly Lundborg, 1952, 1961 Lidén 1953 Wedenberg, 1951 1954) or on fixed-frequency tracings (in the Nordic countries, for example Palva, 1956, 1957) Reference should be made to Jerger (1960) for a detailed list of those workers who have been concerned with determinations of tracing amplitude When patients with unilateral perceptive hearing loss are tudied, it i necessary in most cases to mask the unaffected ear when ordinary head telephones are employed Some workers do n t mention the masking at ll while others restrict their comments to n ting that the

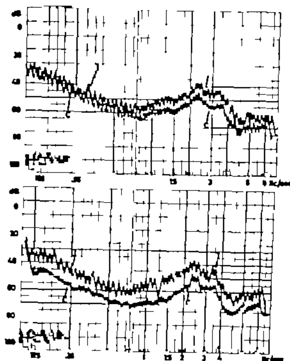


Fig. 6

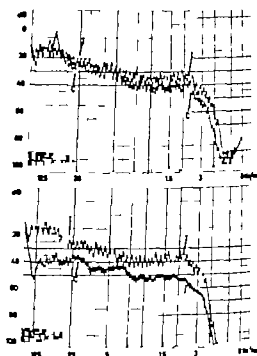


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we calculated the relation between the "C" and "I" amplitudes in the 0 dB as well as in the 80 dB masking condition, and by means of the *t*-test we examined whether mean inter-condition differencies were significantly different from zero. Only the results for 250 and 1000 cps were analysed, but the changes with masking proved statistically significant at both frequencies ($P < 1\%$ and $< 0.1\%$ respectively). Bilger (1965) has examined a material of patients with otosclerosis, in whom the cochlear function ranged from normal to severely impaired. The studies were limited to fixed-frequency recordings at 4000 cps, but comprised extensive statistical calculations of the mutual correlation between the threshold for "I", the threshold for "C", the tracing amplitude for "I" and the tracing amplitude for "C". Bilger came to the conclusion that the only reliable classification of Békésy fixed frequency audiograms into the categories of pathological and normal cochlear function is based on the width of the continuous tone tracing. The mean tracing amplitude was determined during the latter half of a 2 minute tracing. In the present study no significant difference was found between tracing amplitude without and with masking during the 2nd minute of continuous tone tracings at 4000 cps (respectively 4.22 and 3.92 dB). However, it is interesting that in young normal listeners we found a mean amplitude of only 3.74 dB during the 2nd minute, when the contralateral ear was masked at 70 dB SPL noise (without masking, the value was 5.85 dB) (Blegvad, 1967).

In the present study it has not been the intention to throw doubts on the diagnostic value of Békésy audiometry. The contribution of the Jerger procedure to the diagnosis of retro-cochlear lesions is well established (Johnson 1965). We merely wish to draw attention to the fact that no matter which parameter is used in evaluating a Békésy audiogram, the result of the examination will often depend directly on whether the patient's contralateral ear has or has not been stimulated with masking noise during the audiometry.

ZUSAMMENFASSUNG

Die Bekesy-Audiometrie wurde an 81 Patienten mit einseitigem, perzeptivem Hörverlust durchgeführt, teils ohne und teils mit 80-dB-Maskierung des guten Ohres. Sowohl die Töne als auch das Maskierungsgeräusch wurden mit „Insert"-Hörer gegeben. Es ergab sich, dass die Maskierung die Trennung zwischen den „I"- und „C"-Kurven steigert. Ferner verursachte das Geräusch eine hochsignifikante Reduktion der Kurvenausschläge bei frequenzkonstanten „C"-Kurven von 250 und von 1000 Hz und bei frequenzgleitenden „C"-Kurven sowohl im tieferen als auch höheren Frequenzbereich. Bei 7 Patienten wurde durch die Maskierung ein Audiogramm des Jergerschen Typ I zu Typ II geändert, in 7 Fällen wurde Typ II zu Typ IV geändert und in 3 Fällen Typ I zu Typ IV. Auch das Verhältnis zwischen den „I"- und „C"-Kurvenausschlägen wurde geändert. Es wird die Folgerung gezogen, dass, ungeachtet welcher Parameter bei der Beurteilung verwendet wird, das Ergebnis oft von der Einwirkung der Maskierung auf das gegenüberliegende Ohr abhängig ist.

contralateral ear was adequately masked without specification of the intensity of the masking Strangely enough no one appears to have been interested in the influence of masking noise on the results of the study Our investigations show that masking noise applied to the contralateral ear exerts a significant influence on the tracing amplitude both in sweep- and fixed frequency curves

Ever since Jerger's paper in 1960 another aspect of *Békésy* audiometry has attracted increasing attention—namely a comparison between the course of curves recorded with interrupted tone and curves recorded with continuous tone Our studies show that masking also affects the relation between such curves The fact that a type I audiogram is changed to a type II audiograms has of course no significance for the differentiation between diseases of the cochlea and diseases of the acoustic nerve since both types of audiogram occur in cochlear lesions On the other hand, the fact that a type I or type II can be changed to a type IV is more critical, since the first two types are found in cochlear lesions, while according to Jerger type IV is characteristic of an VIIIth nerve lesion It should be mentioned however that according to Myers *et al* (1962) type IV indicates early retro-cochlear defects or a severe cochlear lesion There have also been studies in recent years which have cast doubts on the diagnostic significance of the type IV audiogram (Owens, 1964 Hopkinson, 1966)

In addition to differential diagnosis in cochlear and retro-cochlear hearing loss, Békésy audiometry has been used to distinguish between a normal and a pathological cochlear function From a clinical point of view this is of particular interest in the pre-operative evaluation of patients with otosclerosis. Once again measurement of tracing amplitude on continuous tone tracings has been the procedure previously (Skoog, 1951 Rössler & Lundborg 1954) Such a distinction is only permitted to a limited degree in Jerger's procedure In subjects with normal cochlear function the "I" and "C" curves overlap (type I audiogram) but this also occurs in patients with cochlear hearing loss Type II audiogram on the other hand in which the curves are separated at the higher frequencies is claimed to be characteristic of a cochlear lesion and therefore must be considered pathological In this connection it can be stated that we have found separation between fixed frequency "I" and "C" curves at 1000 and 4000 cps in normal listeners, if the contralateral ear was masked during the audiometry Suzuki & Kubota (1966) have suggested that a comparison be made between the tracing amplitude of the individual for continuous tones and the tracing amplitude for interrupted tones We find that masking the contralateral ear often gives rise to a reduction in the tracing amplitude considerably more pronounced in the case of the "C" tracing than in the case of the "I" tracing In the study by Suzuki & Kubota, the mean tracing amplitude was measured by taking a total of 20 spikes no matter what duration this represented on the tracing In our material this is best compared with our mean tracing amplitude over a period of 2 minutes. In each patient

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DELAYED SPEECH FEEDBACK IN NORMAL HEARING AND CONDUCTIVE HEARING LOSS, WITH AND WITHOUT A FUNCTIONING STAPEDIUS MUSCLE

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Normal ears, otosclerotic ears with normal hearing after stapedectomy and ears with pure conductive hearing loss from otosclerosis and packing of the ear canal, were subjected to a delayed speech feedback test (DSF-test). The results showed no difference in the DSF-effect between the normal ears and the normal hearing operated otosclerotic ears. Neither was there any difference between the non operated otosclerotic and the normal hearing ears with an artificial hearing loss. The results suggest that activity of the stapedius muscle has no influence on the DSF-effect in normal hearing ears and in ears with conductive hearing impairment. The DSF-effect, however, was almost double in the non operated otosclerotic ears and in ears with artificial hearing loss. This may be due to the acoustic energy from the earphones, in the pure conductive hearing losses of about 40 dB, reaching the cochlea both by air and bone conduction in almost equal amounts.

The effect of side-tone-delay (delayed speech feedback) was first noticed by Lee (1950). He showed that when a person's speech was delivered to his ears by a delay line and headphones, it made him stutter, raise his voice and reduce the rate of words (delayed speech feedback phenomenon).

Experimental research on hearing-impaired individuals (Harford & Jerger 1959) indicates that the effect of delayed speech feedback (DSF effect) is influenced by the type of hearing impairment present. In cases of Menière's disease and otosclerosis the DSF-effect is particularly pronounced. In Menière's disease this might be due to the loudness recruitment phenomenon, but in cases of otosclerosis there should be another explanation.

The response of the ear to loud sound and noise activates the stapedius muscle. Contraction of this muscle takes place also when we are talking (Djupesland, 1964, 1965, 1967). The altered frequency characteristics of the ear brought about by this contraction should favour the understanding of speech, especially against background noise (Møller 1962, 1965; Simmons, 1964).

The pronounced DSF-effect noticed in otosclerotics might be due to the stapedius muscle being deprived of its influence on the stapes' position and the frequency characteristics of the ear.

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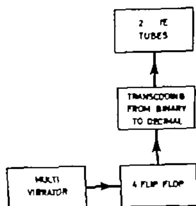


FIG. 1 Simplified block diagram of the stimulus circuit

achieved by the examination of a group of otosclerotics with a fixed stapes and a group of normal hearing individuals in which a conductive hearing los had been introduced by plugging of the ear canal with a cotton wad impregnated with vaseline The wad was placed close to the ear drum and the ear canal filled with model wax. The conductive hearing loss brought about by this procedure approximately equalled that of the otosclerotic group (35–45 dB a.c.)

Eventually the groups with normal hearing and with conductive hearing loss, with and without a functioning stapedius muscle, were compared

The audiological examinations performed in the four groups were pure tone- and speech audiometri and the assessment of the effect of delayed peech feedback on speech

The mean age and sex distribution of the four groups to be compared emerges from Table 1 Apart from the sex distribution in the group "plugged normal ears the groups to be compared are fairly equal

Recruitment of loudness (a.m. Fowler) should be present in none of these groups (Harford & Jerger 1959)

None of the subject examined had any speech disorder or prior experience with DSF-test.

During the examination the subjects read two-digit numbers presented by means of two indicat r tubes as flashing numbers, consecutively changed by means of the stimulu circuit showed in Fig 1

A multi vibrator triggered a decade counter consisting of four "flip flops in series. The signals were transcoded from a binary to a decimal code and fed through manual five steps switch into two cold-cathode indicator tubes (Philips Z 523 M) The tubes were placed 1.5 cm apart on a ch ssis f cing a window (5 cm × 7.5 cm) in the stimulus panel, 1.5 meters in front of the ubject t be examined In thi way five series of ten two-digit numbers were rand mly produced The circuit had no movable parts making noise The presentation speed could be varied from one to four

TABLE 1 *Summary of average error scores and standard deviation median error scores and ranges of individual error scores for each of the four groups at different steps above detection level*

In additi n average age in years, sex distribution and mean air conductio (AC) for the f ur groups.

Test group	Error score: dB-steps above detection level 0	10	20	30	40	50	60	70	80	Age	Sex M	Sex F	Hearing loss (dB), ac
Normal hearing													
Average	1 1	—	3 1	—	6.3	—	9 0	—	11 6	26.9			
St. dev	1.3	—	1.3	—	4 7	—	6 0	—	6.7		5	5	
Median	1 0	—	.5	—	6.5	—	8.5	—	11 0	26.0			
Range	4	—	8	—	14	—	18	—	19				
Otosclerosis (unoperated)													
Average	1 1	3.3	6 6	9 6	12.6	12.9	—	—	—	42.2			
St dev	1 6	5.2	4 4	6.8	7.3	7 6	—	—	—		4	6	35–45
Median	0.5	0.5	6.0	9 5	14.0	12.5	—	—	—	40.0			
Range	5	14	14	21	21	21	—	—	—				
Otosclerosis (operated)													
Average	1.3	2.3	3.8	4 7	7.3	9 1	12.9	—	—	42.1			
St dev	2.5	2.7	4 9	3.6	4 9	5 6	6.2	—	—		4	6	10–15
Median	0 0	1 5	2.5	4 0	6.0	8.5	12.5	—	—	41.5			
Range	8	7	10	11	15	16	18	—	—				
Plugged normal													
Average	1 0	3.5	5.2	8 2	11 0	15.0	—	—	—	25 1			
St. dev	2 0	3.1	6.3	5.8	8.3	7.2	—	—	—		1	9	35–45
Medi n	1 0	3.0	3.5	9.5	10.0	15 5	—	—	—	23.0			
Rang	6	10	19	20	28	26	—	—	—				

The purpose of the present investigation was therefore to elucidate the possible contribution of the influence of the stapedius muscle upon the DSF-effect in normal hearing ears and in ears with conductive hearing loss.

MATERIAL AND METHOD

Examination of listeners differing only with respect to the effect of the contraction of the stapedius muscle should be able to yield an answer to this question

Two groups of 10 listeners with normal hearing were selected one with normal ears, the other with a normal hearing ear after stapedectomy In the latter no effect of the stapedius muscle could be present.

A parallel comparison could be made between individuals with conductive hearing loss with or without a functioning stapedius muscle This was

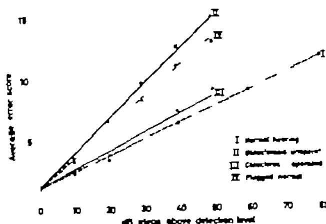


Fig. 3. The erage error score as function of the intensity

tape recorder Only completely correct reproduction of the two-digit numbers were accepted the maximum possible error score thus being 40

Ten normal hearing persons were used for detectability threshold measurements. Each subject read numbers slowly and was asked to report when he first heard his own voice through the earphone During these measurements, the amplifier was continuously monitored by the operator The median of the obtained thresholds served as the reference detectability threshold for the investigation

For the hearing-impaired subjects the hearing loss was compensated by dding the median value of the hearing level at the octave frequencies 250–8000 Hz to the reference detectability threshold.

RESULTS

A emerges from Fig. 3 the normal hearing, operated otosclerotic ears behaved as normal ears, the difference in a erage error score being in significant

The ears suffering from conducti hearing loss brought about by otosclerosi or by plugging of the ear canal showed a significant higher average error score The difference between the two groups with conductive hearing los is, however insignificant. Detailed results are given in *Table 1*

DISCUSSION

The result of the examination show no significant difference in average error score between indi iduals with and without a *functioning stapedius* muscle whether the hearing be normal or a *conductive hearing loss be* present

We may therefore conclude that the action *of the stapedius muscle has* been of no importance *of the* average error score by DSF-test.

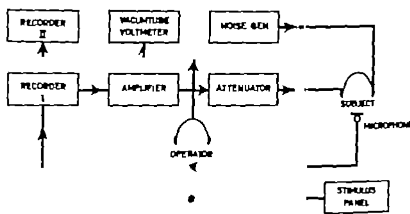


FIG. 2. Block diagram of the equipment used in DSF-test.

numbers per second two numbers per second being used in the test The numbers appeared at the same spot and gave a very clear visual read-out.

Fig 2 shows a simplified block diagram of the equipment used in the DSF test When trying to say the flashing numbers presented the subject's speech was recorded by means of a microphone (Tandberg type TM 2) and a tape recorder (Tandberg model 6) with adjustable distance between record and playbackhead The microphone was placed at a distance of 15 cm in front of the subject and the delay period between the recorded and played back signal was kept constant at 0 17 second which according to Butler & Galloway (1957) is an optimal delay

The output from the tape recorder was fed into an amplifier (Tandberg tape recorder model 3B) then through a matching transformer (5/500 Ω) to an attenuator (Grason and Stadler model 350 A) and finally to a set of earphones (Permoflux PDR 8) In addition the subjects speech was recorded on a second tape recorder (Tandberg model 8) for later study A tube voltmeter (Bruel and Kjær type 2401) was used to control the intensity of the delayed signal For the control listening the operator wore a set of earphones (Brown LTD type K)

At the DSF-examination the delayed speech signals were presented at five sensation levels, 10 20 30 40 and 50 dB above detection threshold In the normal hearing subjects where a higher sensation level could be reached the sensation levels used were 20 40 60 and 80 dB

The delayed speech was always presented to one ear while the contralateral ear was adequately masked by white noise from a white noise generator (Grason and Stadler model 90 S) At each level the subjects were presented a series of 40 numbers (a brief rest period of five second was allowed after 20 numbers) The individual DSF-effect at each sensation level was assessed by the error scores of the speech from the second

ZUSAMMENFASSUNG

Normale Ohren, otosklerotische Ohren mit normalem Gehör nach Stapedektomie und Ohren mit reiner Leitungsschwerhörigkeit (durch Otosklerose oder Packung des Gehörganges verursacht) wurden einem „delayed-speech-feedback" Test unterzogen. Zwischen den normalen Ohren und den nach Stapedektomie normalhörenden otosklerotischen Ohren wurde kein signifikanter Unterschied gefunden. Auch bei den durch Otosklerose rein Leitungsschwerhörigen und denen, die durch Packung des Ohrkanals Leitungsschwerhörige wurden, betrug der Hörverlust rund 40 dB. In beiden Gruppen war die Wirkung des DSF ungefähr dieselbe. Dennoch konnte kein Einfluss des Musculus stapedius auf die Wirkung des DSF nachgewiesen werden. Die DSF-Wirkung war jedoch bei den Leitungsschwerhörigen beinahe doppelt so gross wie bei denen, die normales Gehör hatten. Dies kann darauf beruhen, dass die Cochlea der Schwerhörigen mit reinen rund 40 dB grossen Leitungsverlusten die akustische Energie vom Kopfhörer mit ungefähr derselben Intensität sowie durch Luft als auch durch Knochenleitung empfängt und dadurch einer Verdopplung der Erregung ausgesetzt ist.

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On the other hand individuals with a conductive hearing loss, whether it be caused by otosclerosis or the plugging of the ear canal have shown a significantly higher average error score than the normal hearing ears.

The results obtained in the present investigation in normal and non-operated otosclerotic ears agree well with those published by Harford & Jerger (1959) It must therefore be the conductive hearing loss which, *per se* brings about the higher error score by DSF test

From Table 1 may be calculated the increase of the average error score in relation to the increase of the intensity of the DSF signal delivered through the earphone For the groups with conductive hearing loss, natural or artificial the average error score increases at a rate almost double that seen in the normal hearing ears.

In cases of monotic deafness, cross hearing will take place at about 50 dB delivered from a conventional earphone to the deaf ear (Hirsh, 1952 Langenbeck 1952)

In case of pure conductive hearing loss yielding the conditions necessary for "absolute bone conduction" hearing, air borne sound in the frequency area 125 cps through 1 kc delivered from the earphone may be able to elicit hearing through bone conduction at a dial reading of about 40 dB (Langenbeck 1952)

In pure conductive hearing losses of about 40 dB as in the present investigation the acoustic energy from the earphone may thus reach the cochlea with an almost equal amount by air and by bone conduction, thus doubling the stimulation of the cochlea brought about by the DSF signal Whether or not this may be the explanation to the almost doubling of the average error score in the conductive hearing losses of the present investigation is open to further study

CONCLUSION

The examination of a group of individuals with about 40 dB pure conductive hearing loss caused by fixation of the stapes in otosclerotic ears or massive packing of the total ear canal in normal ears have shown almost the same effect on speech by the delayed feedback of the speech signal through a conventional earphone A group of normal ears and ears with normal hearing after stapedectomy have likewise shown almost the same effect of the delayed feedback signal on the speech The contraction of the stapedius muscle can therefore be of no importance to the DSF-effect.

The delayed feedback effect in the groups with pure conductive hearing loss of about 40 dB was almost twice as large as in the normal hearing groups This may be due to the acoustic energy from the earphone reaching the cochlea with an almost equal amount both by air and by bone conduction thus doubling the delayed feedback effect on the speech Whether this is the explanation or not will be subject to further investigation

(Lucas, 1964 Stuteville & Corley 1967) which implies that the glands of the palate are more frequently the site of tumours than any of the other intraoral salivary glands. The most common sites of adenoid cystic carcinoma are the hard and soft palate the nose and its accessory sinuses, and the trachea and bronchi (Rauch, 1959 Soboroff 1959 Becker 1960 Stewart, 1961)

In previous studies, we have dealt with adenoid cystic carcinoma of the submandibular and parotid glands (Eneroth & Hjertman, 1966 Blanck *et al* 1967) However in comparison to these tumours, adenoid cystic carcinoma located to the palate presents different problems with respect to both diagnosis and prognosis. An account is given in this paper of a series of such tumours occurring primarily in the palate with special attention focused on illustrating the relation between the histological structure of the tumours and their clinical course

Present Series

The present study is based on an analysis of histologically verified tumours of the palate in 383 patients registered at Radiumhemmet during 1909–1960 The greater part of the material was primarily classified according to a nomenclature in which several types of tumour not defined until recent years, were assigned to diffuse collective groups. To enable a histological-clinical correlation study to be carried out a histological re examination was made of the whole material On the basis of this re examination the material was re-classified according to a modern and more differentiated nomenclature than the original one.

The prerequisites for a histological re-examination exist, since the whole tumour material is available at the Institute of Radiopathology Radiumhemmet partly as sectioned specimens and, in most cases as paraffin-embedded material as well Hi tological re-examination of the palatal tumours in the 383 patients disclosed a non-neoplastic condition in 25 a benign tum ur in 139 and a malignant tumour in 219 patients. A salivary-gland tumour w s present in 170 cases It was benign in 95 and malignant in 75 Structures characteristic of adenoid cystic carcinoma were identified in 37 cases. These patient had been treated during the 1922–1968 period

The clinical follow-up study wa based on 32 patients treated in 1922–1961 i e with a minimum observation period of years. The study was continued until J nuary 1 1967 The f llow up examinations of the patients had been made at least once a year Th data on the linical course were available in the record of Radiumhemmet All patients in the 1922–1961 series un lerwent regular follow up examinations for more than 5 years no patient were lost Th observati n period was always counted from the d te of the first histological erification of the tumou

The prognosis of adenoid cystic carcinoma of the palate was in estigated by studying the rate of local recurrence metastasis, mortality and urvival

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ADENOID CYSTIC CARCINOMA OF THE PALATE

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A histological re-classification of 383 tumours primary in the palate showed an adenoid cystic carcinoma in 37 cases. The relative incidence of this type of tumour is considerably higher in the palate than in the submandibular and parotid glands. A distinct difference is present between the prognosis in tumours at these three sites. Thus, the prognosis is best when the adenoid cystic carcinoma is located to the palate and worst when it is located to the submandibular gland The 37 adenoid cystic carcinomas of the palate were divided into two histologically characteristic types of differentiation one with predominance of the cribriform component and one with predominance of the solid component A long-term clinical follow up study disclosed a much better prognosis in tumours with predominance of the cribriform component, as compared to the extremely poor prognosis in tumours with predominance of the solid component. It is pointed out that a histological grading of adenoid cystic carcinoma into high grade and low-grade malignant types is justified and is of clinical significance

Adenoid cystic carcinoma is a type of tumour with characteristic histological features, and one of its localizations is to the salivary glands. According to e.g Thackray & Lucas (1960) adenoid cystic carcinoma more often involves a minor salivary gland than a major one and accounts for 15% and 4% respectively of all tumours at these sites. Adenoid cystic carcinoma is also found in mucous glands of both the upper and lower respiratory tract as well as in lacrimal glands, where—according to Godtfredsen (1948)—it comprises about 50% of all tumours This type of tumour may in addition be encountered in the breast (Stewart, 1961) and in the sweat glands of the skin (Schweissinger 1958)

Although the tumours originating in the various salivary glands have essentially similar histological features, the incidence of the different types of tumour and their prognosis are considered to vary with the localization

The extensive literature on salivary gland tumours deals chiefly with those of the major salivary glands, especially the parotid Few well-documented reports have appeared on tumours of the minor salivary glands This is natural, since about 90% of all such tumours are located to the major salivary glands, as compared to only about 10% in the minor intraoral salivary glands (Seifert 1966)

About 60% of intraoral salivary gland tumours occur in the palate

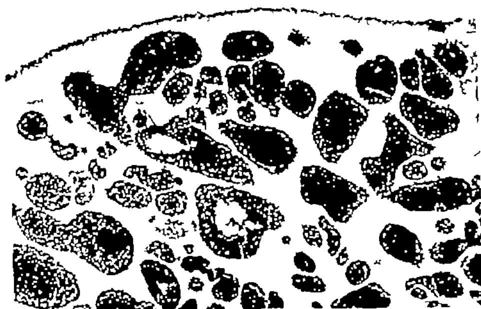


FIG. 2. Adenoid cystic carcinoma of the palate. Poorly differentiated with predominantly solid structures. Photomicrograph × 70.

histologically from those at other sites. The tumour is composed of numerous islands of epithelial cells, presenting a glandular like pattern. These islands form so-called cribriform or cylindromatous structures (Fig. 1) which may however vary in different tumours and also, to some extent, in different areas of the individual tumour. Thus, the epithelial proliferation may appear more or less cystic, or may form predominantly solid cords (Fig. 2). In most cases, however the tumour structure is fairly homogeneous, either predominantly cribriform (highly differentiated type) or predominantly solid (poorly differentiated type).

As a rule the connective tissue surrounding the epithelial structures shows hyalinization. The epithelial cells mostly exhibit moderate nuclear polymorphism and mitoses are generally few. *A relatively characteristic histological feature* of adenoid cystic carcinoma is the lack of encapsulation. Diffuse or tentacular invasive growth into the surrounding tissues is commonly present, and may be an important criterion in the differential diagnosis from non-malignant tumours, such as pleomorphic or monomorphic adenomas of various types.

Clinical features

Of the 37 patients with adenoid cystic carcinoma of the palate 19 were men and 18 were women, i.e. no sex difference was present. The age of the patients at the time of histological verification of the tumour and treatment ranged from 27–83 years (mean 6.0 years). The mean age of the

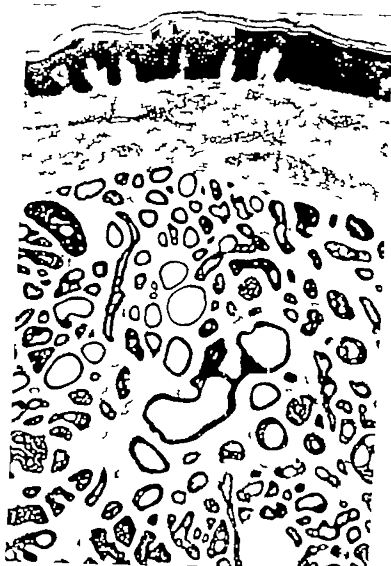


Fig. 1 Adenoid cystic carcinoma of the palate Highly differentiated with cribriform structures. Photomicrograph × 70

rate The survival rate is based on determinate groups The survival rate of the determinate group excludes indeterminate patients, i e those lost to follow up and those who died without signs of tumour disease As already stated no patients in the present series were lost to follow up Thus, the grade of malignancy of adenoid cystic carcinoma was evaluated by studying the determinate survival rate which is based on the mortality in the tumour disease Since patients with adenoid cystic carcinoma occasionally have a long survival a long observation period is necessary to obtain reliable prognostic figures In the present series, the follow-up period ranged from 5 to 44 years

Histological features

The histological features of adenoid cystic carcinoma are now well known (e.g Thackray & Lucas, 1960) Such tumours of the palate do not differ

TABLE 2. *Interval between treatment and first local recurrence in 12 cases of adenoid cystic carcinoma of the palate*

Interval, years	No. of patients
0–1	3
2–5	3
6–10	3
10	3
Total	12

the surgical procedure in these cases is rather to be denoted as a biopsy. An operative intervention of varying extent was performed in 27 cases. In 7 cases the bony palate was resected, and neck dissection was undertaken in 2 of 3 cases with palpable lymph-node metastases. In the third case only irradiation treatment was given to the metastases. In the 21 cases in which surgical and roentgenological treatment were combined, irradiation was given preoperatively in 9 cases, postoperatively in 10 and both pre- and postoperatively in 2 cases.

Prognosis

Recurrence

A local recurrence after the first treatment occurred in 12 of the 32 patients followed up for more than 6 years. The interval between treatment and the first local recurrence can be inferred from Table 2. In 3 cases, a local recurrence did not take place until after 13, 20 and 23 years, respectively. More than one recurrence occurred in 3 cases. In the first case the tumour recurred after 13 and 27 years, in the second after 5 and 8 years, and in the third case 6 recurrences took place during a period of 4–9 years after the first treatment. Altogether 8 of the 12 patients with a local recurrence died of the tumour disease. Totally 20 patients had no local recurrence and only 4 of them died of the tumour disease.

Metastasis

Metastases were demonstrated in 11 of the 32 cases followed-up for more than [illegible] years. In 3 of the 11 cases, metastases were already present at the first examination, whereas in the other 8 they appeared later. In 3 patients there were both regional lymph-node metastases and distant metastases, in 4 regional lymph-node metastases only and in the remaining 4 distant metastases alone. Thus, regional lymph-node metastases and distant metastases were observed in totally 7 cases each. Distant metastasis was to the lungs in 7 cases, to the skeleton in 3, to the liver in one and to the kidney in one. In 3 cases, distant metastases were present at more than one site. The interval between the first symptom of the tumour and appearance

TABLE 1 *Interval between first symptom and treatment of adenoid cystic carcinoma of the palate*

Interval years	No. of patients
0–1	23
2–3	6
4–5	5
> 5	3

patients with a highly differentiated adenoid cystic carcinoma was 59 1 years the corresponding figure in those with a poorly differentiated tumour was 48 8 years.

The interval between appearance of the first symptom of the tumour and its treatment ranged from a few days to 12 years with a mean duration of 1 9 year (Table 1) In 23 cases the duration was less than 1 year and in only 3 cases was it more than 5 years. A lump in the palate was the commonest symptom of the tumour it was present in 26 cases, and was the only symptom in 11 Pain ulceration and bleeding occurred in 10 6 and 1 case respectively Three patients consulted a dentist because of a swelling in the palate which created difficulty in wearing their dentures, and in 5 cases the lesion was detected by a dentist without the patient having had any complaints Speech and eating difficulties, blocked nasal passages and a bilateral swelling on the neck were present in one case each

In 24 cases the tumour was localized to the hard palate, in 9 to the soft palate and in 4 cases to both the hard and soft palate Extension beyond the palate was present in 8 cases, 5 of them with primary localization to the hard palate and 3 to the soft palate Extension from the hard palate to the nasal cavity occurred in 3 cases and to the maxillary sinus and maxillary alveolar process in one case each Extension from the soft palate to the nose lateral pharyngeal wall and the tonsil had taken place in one case each

Although data on the size and appearance of the tumour were incomplete in some cases they showed that in many cases the tumour was advanced even at the first examination In 24 cases the diameter of the tumour was 2 cm or more The surface of the tumour was stated to be ulcerated in 13 cases At the first examination palpatorily definite cervical lymph node metastases were considered to be present in 3 cases bilaterally in 2 of them.

Treatment

During the period covered by the present series, the patients were not treated uniformly Treatment was surgical or roentgenological or a combination of the two forms Altogether 31 of the 37 patients received irradiation treatment and in 10 of them this was the only actual treatment since

TABLE 5 *Interval from first symptom of primary tumour to death from carcinoma in 12 cases of adenoid cystic carcinoma of the palate*

Survival time, years	0–3	4–5	6–10	11–15	>15
Highly differentiated adenoid cystic carcinoma, no. of cases	0	0	4	1	2
Poorly differentiated adenoid cystic carcinoma, no. of cases	5	0	0	0	0

on the basis of the relative occurrence of the respective components. Thus, the tumours were divided into two groups according to their histological features. The distribution of these two groups in the 32 patients who could be followed-up for at least 5 years is seen in Table 4 It is evident from this table that 7 of the 25 patients with a highly differentiated adenoid cystic carcinoma died of the tumour disease the corresponding incidence in those with a poorly differentiated tumour being 5 of 7

Five patients with a highly differentiated tumour were alive at the last follow-up examination, 5 9, 1 27 and 29 years, respectively after the first treatment. One patient with a poorly differentiated tumour was also alive on this occasion 3 years after treatment The interval between the first symptom of the primary tumour and death in the tumour disease (survival time) provides a measure of the malignancy of the tumour The survival time f patients who died of adenoid cystic carcinoma of the palate is seen in Table 5 The survival time was less than 3 years in all patients with a poorly differentiated tumour whereas it exceeded 5 years in all those with a highly differentiated tumour The best conception of the prognosis in a cert in type of tumour is, however obtained by a study of the survival rate, nd particularly of the determinate survival rate

Table 6 shows the determinate survival rate after 5 10 15 and 20 years observ tion in th whole series of patients with adenoid cystic carcinoma, without taking into account the hi tological subgroups. Altogether 32 pa

TABLE 6 *Adenoid cysti carcinom of the pal te 5–20 years follow-up study*

Observation period (years)	No. of patients	Died of: Tumour disease	Died of: Intercurrent disease	Lost to follow-up	Determinate survival rate: No. of patients	Determinate survival rate: No. of survivals	Determinate survival rate: % of survival
5	32	5	7	0	25	20	80
10	27	10	10	0	18	8	44
15	24	10	8	0	16	6	38
20	18		7	0	11	4	36

TABLE 3 *Interval between first symptom of the tumour and appearance of metastases in adenoid cystic carcinoma of the palate*

	No of patients	
Interval, years	Regional lymph node metastases	Distant metastases
0–5	3	3
6–10	1	2
11–15	2	1
16–20	1	1

of metastasis varied greatly (Table 3) In 3 cases regional lymph-node metastases were not demonstrated until more than 10 years after onset of the primary tumour this applied to distant metastases in 2 cases

Survival

The prognosis was investigated chiefly by studying the mortality in the tumour disease and the survival rate To permit reliable conclusions to be drawn from the clinical follow up study this was based on a series of cases with a long observation period The series thus comprised 32 patients treated during the period 1922–1961 all of whom were followed-up until 1967 i e., for 5–44 years

As previously stated adenoid cystic carcinoma can be divided into two histologically characteristic types of differentiation one with a predominance of the cribriform component and one with predominance of the solid component We have considered these structural components to represent different grades of maturation (differentiation) of the tumour tissue the cribriform structure representing highly differentiated tumour tissue and the solid structure poorly differentiated such tissue

An attempt was made to grade the malignancy by grouping the tumours

TABLE 4 *5–44 years follow-up study of 32 patients with adenoid cystic carcinoma of the palate*

		Died of	
Histological features	No of patient	Tumour disease	Intercurrent disease
Cribriform structure (highly differentiated)	25	7	13
Solid structure (poorly differentiated)	7		1
Total	32	12	14

TABLE 9 *Adenoid cystic carcinoma*

Compariso betwee the determinat survival rate with tumour t different sites.

Follow-up period, years	Determinate survival rate % Palat	Parotid gland	Submandibular gland
5	80	73	50
10	44	39	25
15	34	21	0
20	36	13	0

palate in 383 patients registered at Radiumhemmet during 1909–1966 The incidence of adenoid cystic carcinoma in the salivary glands of the palate is of particular interest, since we were able in previous investigations of tumours of the parotid gland (Blanck *et al* 1967) and the submandibular gland (Eneroth & Hjertman 1967 Eneroth *et al.*, 1967) to study the incidence of adenoid cystic carcinoma in the major salivary glands. Adenoid cystic carcinoma wa found to account for 2 1% of all salivary-gland tumours of the parotid gland, and for 15.2% of those of the submandibular gland. Of the malignant salivary-gland tumours of the palate parotid gland and submandibular gland adenoid cystic carcinoma comprised 49.3, 11 7 and 40.3% respectively

In a survey of several series of palatal tumours made by Chaudhry *et al* (1961) and in a study by Stuteville & Corley (1967) adenoid cystic car inoma amounted to 42 4 and 57 1% respectively of the malignant salivary gland tumours. These figures are in good agreement with the incidence in th present series The incidence of adenoid cystic carcinoma varies greatly t different sites. It can be seen to be high in the minor salivary glands of the palat as compared to the submandibular gland and, especially to the parotid gland N sex difference existed in our series. Stuteville & Corley (1967) on the other hand, reported a preponderance of female patients. N significant sex difference was present either in our series of adenoid cystic carcin ma f the submandibular gland (Eneroth & Hjertman, 1968) f the parotid (Blanck *et al* 1967) The mean age of patients with a highly differentiated and a poorly differentiated adenoid cystic carcin ma f the pal t respecti ely was 59 1 and 48.8 years. The difference between th mean age in these two gr ups wa thus a high as 10.3 years Four of the patient with a poorly differentiated tumour were les than 40 years ld

Aden id cystic carcinoma is regarded to be a slowly growi g tumour with a long d ration of the sympt ms before it is diagnosed (Moran *et al* 1961) In our previou studies of this tumour in the parotid (Blanck *et al* 1967) and the ubmandibular gland (Eneroth & Hjertm n, 1966) the pre operative duration of the symptoms wa found to be a mean 3 7 and 5.6

TABLE 7 *Poorly differentiated adenoid cystic carcinoma of the palate 5–20 years follow-up study*

	Died of				Determinate survival rate		
Observation period (years)	No of patients	Tumour disease	Intercurrent disease	Lost to follow up	No of patients	No. of survivals	% of survivals
5	7	5	1	0	6	1	17
10	0	5	1	0	5	0	0
15	0	5	1	0	5	0	6
20	5	4	1	0	4	0	0

tients had been under observation for 5 years, 28 for 10 years, 24 for 15 years and 18 for 20 years The determinate survival rate shows a pronounced decrease from 80% in the 5 year group to 44% in the 10-year group after which it remains practically constant i.e., 38% and 36% respectively in the 15 year and 20 year groups

The determinate survival rate can also be calculated separately for the two tumour groups differing with respect to histological features. It is then found that the determinate survival rate of poorly differentiated adenoid cystic carcinoma is 17% in the 5 year group and 0% in the 10-year group (Table 7) whereas the corresponding figures for highly differentiated adenoid cystic carcinoma are 100% in the 5-year group and 62% in the 10 year group (Table 8)

DISCUSSION

The palate is stated to be the commonest localization of the relatively rare type of tumour known as adenoid cystic carcinoma Consequently a histological and clinical study in a large series of such tumours at this site is of great value for assessing the biological properties of this type of tumour

The 37 cases of adenoid cystic carcinoma in the present series comprise 9 7% of the total number and 21 8% of all salivary gland tumours of the

TABLE 8 *Highly differentiated adenoid cystic carcinoma of the palate 5–20 years follow-up study*

	Died of				Determinate survival rate		
Observation period (years)	No of patients	Tumour disease	Intercurrent disease	Lost to follow-up	No of patients	No of survivals	% of survivals
5	25	0	6	0	10	19	100
10	22	5	9	0	13	8	62
15	18	5	7	0	11	6	55
20	13	3	6	0	7	4	57

sistently to be best when the tumour is located to the palate, and worst when it is located to the submandibular gland A common feature of the prognosis of adenoid cystic carcinoma at all three sites is that the deter minate survival rate after 10 years is only half as high as after 5 years With an observation period exceeding 10 years, the rate is relatively un changed in adenoid cystic carcinoma of the palate whereas when the parotid and submandibular glands are involved it continues to fall

In the 37 adenoid cystic carcinomas of the palate, the typical structural components—cribriform and solid—were present in varying proportions in the individual tumours We considered these structural components to represent different grades of differentiation of the tumour tissue the cribri form structure representing high differentiation and the solid structure poor differentiation The tumour was highly differentiated in 29 cases, and poorly differentiated in 8 Our study of the correlation between structural type and clinical course showed that tumours with predominantly solid structures were associated with higher mortality in the tumour disease (Table 4) and, especially shorter survival time (Table 5) than tumours with predominantly cribriform structures. The determinate survival rate after 5 and 10 years observation was 17 and 0% respectively in the poorly differentiated group (Table 7) and 100 and 62% respectively in the highly differentiated group (Table 8) Consequently we consider it justified to classify adenoid cystic carcinoma of the palate—on the basis of the histological features—into a high malignant and a low malignant type The high malignant type is associated with an exceedingly poor prognosis, wherea that of the low malignant type is much more favourable

ZUSAMMENFASSUNG

Eine histolog sche Unkl suf ierung on 383 Tumoren primä im Gaumen ergab n 37 Fallen in adenoid zystisches Karzinom. D s relati Vorkommen dieses Tumors pa ist bedeutend höher im Gaumen al in der Gl. submandibularis und der Gl. parotis. E besteht ein deutli her Unterschied in der Prognose der Tumoren n diesen d Lokal sationen. Die Prognose ist am besten, wenn das ad noid-zy tische Karzinom im Gaumen lokal iert ist und am schlechtesten bei Lok lisation n der Gl. submandibula is. Die 37 aden id-zystischen Karzinome im Gaumen wurden in zwei h st logisch harakteristische *Typen der Differenzierung* ngel lt ei Typ mit Vorherrschen der cribrif rmen Komponente u d iner mit Vorherrschen der soliden Komponent Eine Studie über ein langfristige klin sche Nachkontrolle ergab i e viel bessere Prognose der Tumoren mit Vorherrschen der cribriformen Kompon nte im Vergleich zu der äusserst schlechten Prognose der Tumoren mit Vorherrschen der soliden Komponente Es wird her orgehoben, d s ein histologische Unterl ilung des adenoid-zystischen Karzi n m in hoch- nd geringmalige Typen berechtigt i t und ein klinische Bedeu t ng h t.

years respectively The considerably shorter duration of the symptoms in the present series—1 9 year—might indicate that adenoid cystic carcinoma of the palate is not a slowly growing tumour Another possibility is that the tumour may exist in the palate for a long time before it produces symptoms that are noticed by the patient It is difficult for the patient to inspect the palate himself Five patients whose tumour was detected by a dentist had no history of symptoms, despite the tumour being 1.5 × 2.5 cm up to twice this size As a rule, the palatal tumours caused few symptoms, irrespective of an advanced extent The commonest ones—a lump in the palate and pain—were present in 70 and 27% respectively of the cases.

More than $^2/_3$ of the adenoid cystic carcinomas in the present series were located to the hard palate A similar difference between the hard and soft palate with respect to salivary gland tumours has been reported earlier by Martin (1942) and Renstrup & Pindborg (1960) As far as squamous-cell carcinoma is concerned the former author stated that it was, on the contrary more *often located to the soft palate Adenoid cystic carcinoma* is a type of tumour known to be associated with a high incidence of recurrence In our series, a local recurrence took place in 12 of 32 patients followed up for at least 5 years The interval between primary treatment and appearance of a recurrence ranged from less than 1 year to 23 years The long follow-up period in our series is of great value for assessing the tendency of adenoid cystic carcinoma to recur Altogether $^2/_3$ of the patients with a local recurrence died of the tumour disease whereas this applied to only $^1/_3$ of those who had no recurrence Thus, local recurrence seems to be accompanied by an exceedingly poor prognosis

Metastases were demonstrated in 34% of the patients who were treated for adenoid cystic carcinoma of the palate and followed up for more than 5 years In our earlier series, the incidence of metastasis of this type of tumour was 43% in the parotid (Blanck *et al* 1967) and 7o% in the submandibular gland (Eneroth & Hjertman 1966) The duration of the symptoms before treatment of the tumour was a mean 1 9 year in the palate 3 7 years in the parotid, and 5 6 years in the submandibular gland A long interval between onset of the symptoms and treatment thus seems to increase the risk of metastasis. The interval from the first tumour symptom to demonstration of metastasis may be extremely lengthy i e., in the present series it was from 10 to 20 years in 4 cases This further emphasizes the necessity of a long observation period for evaluating the prognosis in adenoid cystic carcinoma

A good conception of the prognosis is obtained by a study of the determinate survival rate A comparison between the prognosis of adenoid cystic carcinoma at different sites is of interest We have previously given an account of adenoid cystic carcinoma of the parotid (Blanck *et al.*, 1967) and of the submandibular gland (Eneroth & Hjertman, 1966) and it can be seen in Table 9 how the prognosis, based on the determinate survival rate differs with a tumour at these sites and in the palate The prognosis appears con

Acta oto-laryngologica 66, 261-272 (1968)

CORTICAL RESPONSES TO ROTATION

II. Responses Recorded at the Onset of Rotation from the Second Somatic Sensory and Posterior Areas

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Using a Mnemotron computer a method h been developed permitting on t study in cat the cortical responses appearing when angular a leration is started. According t this method the entrance of laby ri thin impulses is not restricted to th second somatic sensory rea (S_2) but e te d posteriorly chiefly into part of the auditory cortex and int the so-c lled sociation corte (gyrus suprasylvius mediu). At least i some f th experiment the anterior part of the gyrus ectosyl ius posterior d the posterior corner f the gyrus suprasyl in medius (part of the second sual area) showed responses f rel ti ely short latency. General m sele paralysi or bilateral blation of S_2 did n t pre ent such responses in posterior parts f the hemisphere while b lateral labyri thect my abol shed them.

In the preceding experiments (part I) chiefly diffuse cortical reactions appeared foll wing cessation of rotati n alth ugh in some instances, par ticularly in man th re ponses from posterior parts of the hemispheres were more marked. The diffuse appearance of the responses uggested that th impulses from the vestibular nu lei were prop gated to the reticular f rmation nd th t subsequently the diffuse thalamic projection system w acti ated. Fu therm re one h to bear in mind that the angular ac celerati n during the ingl rotations induces a stimulati n of the labyrinth nd consequently cortical excitation so that the cortical response elicited by u lden d celeration (topping f th rotation) would be uperimposed pon th tat of excit ti n in luced by the preceding accelerati n. It seemed, therefor desirable t tudy th cortical responses to the onset of the rot tion from th resting state.

MATERIAL AND METHOD

Twenty ix at kept under nemb utal (3-12 mg kg) and chloral se (25 mg kg nesthesia were tightly hel l on n animal board that was fixed

This ork as pported by Gra t N. 01418, N tion l Instit t for Neurological Dise ses nd Blindness, N tional I stitutes of Health, U.S.P.H.S.

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CORTICAL RESPONSES TO ROTATION

II Responses Recorded at the Onset of Rotation from the Second Somatic Sensory and Posterior Areas

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Using a Mnemotron computer a method has been developed permitting one to study in cats the cortical responses appearing when angular acceleration is started According to this method the entrance of labyrinthine impulses is not restricted to the second somatic sensory area (S_2) but extends posteriorly chiefly into parts of the auditory cortex and into the so-called association cortex (gyrus suprasylvius medius) At least in some of the experiments the anterior part of the gyrus ectosylvius posterior and the posterior corner of the gyrus suprasylvius medius (part of the second visual area) showed responses of relatively short latency General muscle paralysis or bilateral ablation of S_2 did not prevent such responses in posterior parts of the hemisphere while bilateral labyrinthectomy abolished them.

In the preceding experiments (part I) chiefly diffuse cortical reactions appeared following cessation of rotation although in some instances, particularly in man, the responses from posterior parts of the hemispheres were more marked The diffuse appearance of the responses suggested that the impulses from the vestibular nuclei were propagated to the reticular formation and that subsequently the diffuse thalamic projection system was activated Furthermore one has to bear in mind that the angular acceleration during the single rotation induces a stimulation of the labyrinth and consequently a cortical excitation so that the *cortical response elicited* by sudden deceleration (stopping of the rotation) would be superimposed upon the state of excitation induced by the preceding acceleration It seemed, therefore, desirable to study the cortical responses to the onset of the rotation from the resting state

MATERIAL AND METHOD

Twenty six cats kept under nembutal (3–12 mg/kg) and chloralose (25 mg kg) anesthesia were tightly held on an animal board that was fixed

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Fig. 1. Averaged responses of cat left cortical areas to onset of 10 cw. t. rclockwise rotation. Electrode placement are shown terior part f Fig. 1 a. Chloralose-sod. m pentobarbital anesthesia in this and subsequent experiments, if not otherwise indicated. Analysis sweep time 500 msec, time marked 50 msec. Calibration 25 V (applies also to subsequent records)

pairs of electrodes (1–2 *a*, 2 *b*–3) when the area under the electrodes **2** *a*, **2** *b* corresponded to the site of the evoked potential. These initial responses were *usually followed by slow polyphasic fluctuations*, their first peak appeared over 50 to 150 msec following the stimulus or even later.

It should be emphasized that such responses were not limited to the

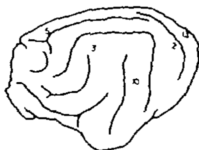


Fig. 1. Diagram showing electrode placement corresponding to Fig. 1 [illegible] anterior part and to Fig. 4 in posterior part. *Anterior row of electrodes*: *1* Gyr. [illegible]ylv post.; 2, gyr. syl[illegible] upper part; *3* corner between gyr. ectosyl[illegible] and med.; *4* corner between gyr. suprasyl[illegible] and med.; *5*, anter. part of gyr. lateral. *Posterior row of electrodes*: *10* Gyr. ectosylv. post.; *11* and 12, gyr. suprasylv. post.; *13* gyr. lateral. post.

to a rotating disc (radius 35.5 cm) with the cat s head close to the center of the disc The rotation was produced by a weight of 100 gm that acted by means of a string carried over an upper and lower pulley and along the grooved periphery of the disc to which its free end was attached.

Again the responses evoked by single rotations (in this case by the onset of the rotations) were averaged by a Mnemotron computer Its principle was explained in part I of this study A special switch started the rotation and triggered the computer with an average time interval of 4.5 msec between the onset of the sweep of the computer and the start of the rotation [1]

In order to determine the angular acceleration at the beginning of rotation a small stationary electric bulb was placed below the rotating disc close to its periphery and opposite to it a photoelectric cell To the periphery of the disc a photographic film was attached on which a series of equidistant vertical lines had been photographed The light of the bulb passed through the film with the vertical lines and activated the photocell the latter s current was conducted to one of the inputs of the computer From the records showing the fluctuations of the output of the photocell at angular displacements of 0 05 the angular velocities and the angular accelerations were determined The acceleration gradually increased until a constant value of 40 /sec² was reached after 10 20 40 60 and 80 msec respectively the angular accelerations were 5 10 18 5 26 and 30 /sec²

Since monopolar recordings did not permit a localization of foci of cortical responses bipolar derivations were used the electrodes (stainless steel balls as described in part I) being placed in straight rows (see Fig 1 a) equidistant as far as possible

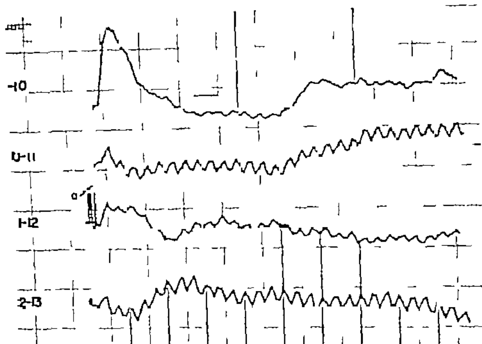
RESULTS

Using the averaging technique it could be shown that the starting of angular acceleration induced evoked potentials in the cerebral cortex

Responses from the second somatic sensory area

From the gyrus ectosylvius anterior and the gyrus suprasylvius anterior (Figs 1 and 1 a) responses could be recorded 14 times, while adjacent leads yielded no or smaller reactions Peak latencies between onset of rotation and peak of the response varied between less than 10 msec and over 50 msec (see Table 1) The voltage of these responses varied betwen 10 and 70 µV Most responses lasted between 20 and 60 msec in one instance a duration of 10 msec in another of 100 msec was observed In 6 instances phase reversals were noticed i e deflections in opposite direction in two adjacent

The design of thi s tch will be gladl pplied upon request
We wish to expres ur deep ppreci ti n t Dr G H nov nd M G \ J cobr for their advice regarding these phys al problems.



Fm. 2. A eraged responses t onset of 10 counterclockwise rotations. Electrode positions re bow in F g. 2 a. Gallamine triethiodide paraly is besides chloralose sodi m pento-barbital nesthesia. a, Artifact.

and the upper part of the gyrus suprasylvius posterior (corresponding to part of the so-called second visual area) could be compared with those in the gyrus ectosyl ius posterior in 20 instances. The responses in the latter gyrus had a higher amplitude than those in the adjacent parts of the gyrus suprasylvius in 16 cases, i e 4/5 of the cases twice there was no definite difference in the amplitude of the evoked reactions in these two areas, and

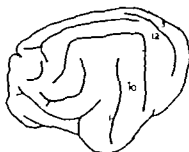


Fig. 2 a. Diagram showing electrode position corresponding t record i *Fig. 2. 1* Sulc ectosyl post.; *10* nd *11* gyr ectosyl post. 12, corner between gyr supra yl med. nd post.; *13*, corner bet een lateralis med. nd post.

TABLE 1 *Responses evoked at onset of rotation*

	2nd somatic sensory area (no. of observations)		Gyrus or sulc. ectosylv. post. (no. of observations)
Peak latent period msec		msec	
<10–15	2	10–15	2
16–25	6	16–25	13
26–40	5	26–40	8
>50	1	No response	1
Voltage, μV		μV	
10–20	3	<20	4
30–40	4	20–40	11
40–50	4	41–60	
60–[illegible]0	3	110	1
Duration, msec		msec	
10	1	<20	1
20–60	12	20–60	14
100	1	61–100	5
		110–200	3

second somatic sensory area. The zone from which phase reversals could be obtained extended, at least in some instances, posteriorly, particularly to parts of the auditory cortex and to the gyrus suprasylvius medius, the association cortex of Buser *et al.* (1959). Phase reversals were noted from the gyrus sylvius anterior (twice), from the gyrus sylvius medius (6 times), from the gyrus sylvius posterior (once), from the gyrus ectosylvius medius (6 times), and from the gyrus suprasylvius medius (3 times).

Responses from the posterior part of the hemisphere

Special attention was paid to the question whether such responses could also be recorded from posterior parts of the hemisphere, particularly from the gyrus ectosylvius posterior and the posterior part of the gyrus suprasylvius medius.

Among 24 cases in which one or both electrodes were found at autopsy in the gyrus or sulcus ectosylvius posterior, in 23 a definite evoked potential (Figs. 2 and 2 *a*) and only in one no response was demonstrable. Phase reversal was found in seven instances (four times from the sulc. ectosylvius posterior, three times from anterior parts of the gyrus ectosylvius posterior) (Fig. 4). No phase reversal was noted from the posterior part of this gyrus. The peak latencies lasted from 10 to 40 msec. The voltage varied from below 20 μV to 110 μV (Table 1). Most responses lasted for 20 to 60 msec.

The responses in the posterior part of the gyrus suprasylvius medius

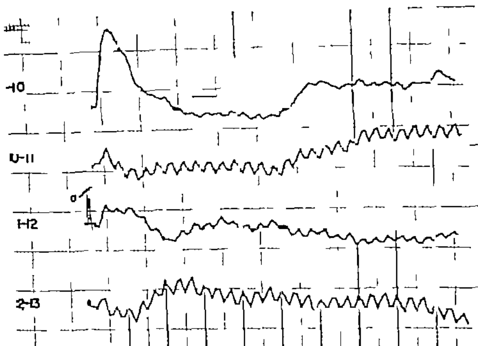


Fig. 2. A eraged responses t onset f 10 cou terclockwise rotations. Electrode positions are show in Fig. 2 a. Gallamine triethiodide paralysi besides chloralose sodium pentobarbital nesthesia. Artifact.

and the upper part of the gyrus suprasylvius posterior (corresponding to part of the so-called second visual area) could be compared with those in the gyrus ectosylvius posterior in 20 instances. The responses in the latter gyrus had a higher amplitude than those in the adjacent parts of the gyrus suprasylvius in 16 cases, i.e., 4/5 of the cases twice there was no definite difference in th amplitude of the evoked reactions in these two areas, and

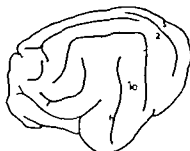


Fig. 2 a. Diagram showi g electrode positions corresponding t record i Fig. 2. 1 Sulc ectosyl post.; 10 nd 11 gyr ectosyl post. 12, corner bet een gyr uprasyl med. and post. 13, corner between gyr lateralis med and post.

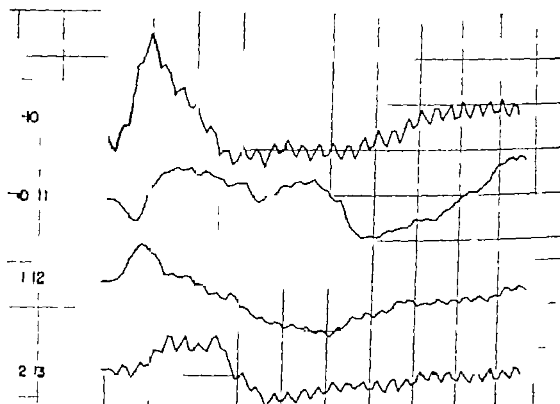


Fig. 3 Cat with bilat ral bl tion of th gyru ecto- d uprasylvi anterior A eraged responses t onset of 10 count rlockwi e rotati ns, with phase re ersal at the corner between the middle and post rio part of the sulc suprasylviu (at *11*) Other electrode positi ns *1* At th gyrus sylvius post rio lose to the lower part of the sulcu ecto- ylvius posteri r *10* gyrus ectosylviu post i r upper part *12* gyrus prasyl ius, corne between middle and posterior part *13* gyrus lat ralis, corner betwee middle and post rior p rt

once there was no response in the posterior part of the gyrus suprasylvius medius In one instance only a higher amplitude (68 μV) was found in the posterior part of the gyrus suprasylvius medius than in the gyrus ectosylvius posterior (26 μV) In this instance the cat was awake but immobilized by gallamine triethiodide under subsequent chloralose-nembutal anesthesia, the reaction from both areas was diminished to 20 μV The peak latencies of the suprasylvian responses varied from 10 to 60 msec Again the majority of the responses lasted for 20 to 60 msec Phase reversal was observed once from the corner between sulc suprasylvius medius and posterior (Fig 3) and once from the sulc suprasylvius posterior The peak latencies in the records showing these phase reversals were 27 and 50 msec respectively

Uncertain effect of direction of rotation

The responses elicited e.g., in the left cerebral cortex were rather similar on clockwise and counterclockwise rotation Small differences of amplitude e g., sometimes smaller amplitude on clockwise than on counterclockwise

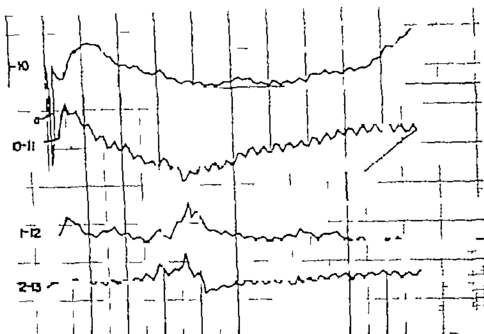


Fig. 4 Influence of bil teral labyrinthectomy pon eraged responses t onset of 10 counterclockwise rotati ns. Fig 4 show responses before and Fig. 4 2 hours fter limination of both labyrinths. Electrode positions re as show I Fig. 1 (*posterior part*)

rotation, could not be explained by the difference in the direction of rota tion (clockwise or counterclockwise) nor was there a regular influence of the sequence of the series of rotations in that the second series induced in some cases a lower in othe instances a higher averaged potential

Control experiment

It wa ascertained whether afferent impulses from contracting skeletal muscles played a part in the production f these responses. Thus rotations were performed in animals immobilized by gallamine triethiodide (flaxedil) either in the waking state or in chloralose-nembutal anesthesia. Abolition of muscula contra tions by flaxedil did not prevent the cortical responses (Fig 2)

In further control experiments the response to 10 averaged partial rota tions was compared with th effect of triggering th sweep f the computer 10 times in order to compare the effects of acceleration with that of ac cidental noises. Th t iggering f the sweep without accelerations, induced only minim l fluctuations of the base line that could not be considered ev ked responses.

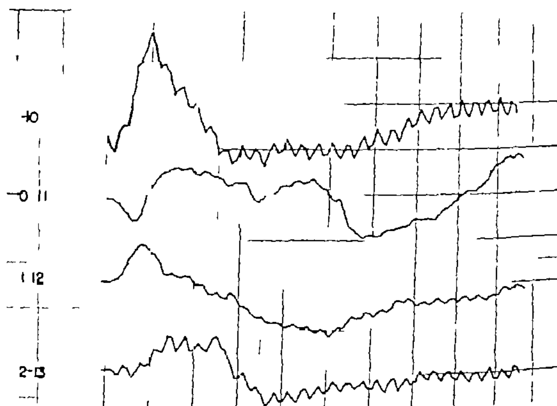


FIG. 3 Cat with bilateral ablation of the gyrus ecto- and suprasylvius anterior. Averaged responses to onset of 10 counterclockwise rotations, with phase reversal at the corner between the middle and posterior part of the sulc. suprasylvius (e.t. 11). Other electrode positions: 1, At the gyrus sylvius post. 1 close to the lower part of the sulcus ectosylvius posterior; 10, gyrus ectosylvius posterior upper part; 12, gyrus suprasylvius, corner between middle and posterior part; 13, gyrus lateralis, corner between middle and posterior part.

once there was no response in the posterior part of the gyrus suprasylvius medius. In one instance only a higher amplitude (68 μV) was found in the posterior part of the gyrus suprasylvius medius than in the gyrus ectosylvius posterior (26 μV). In this instance the cat was awake but immobilized by gallamine triethiodide; under subsequent chloralose-nembutal anesthesia, the reaction from both areas was diminished to 20 μV. The peak latencies of the suprasylvian responses varied from 10 to 60 msec. Again the majority of the responses lasted for 20 to 60 msec. Phase reversal was observed once from the corner between sulc. suprasylvius medius and posterior (Fig. 3) and once from the sulc. suprasylvius posterior. The peak latencies in the records showing these phase reversals were 27 and 50 msec respectively.

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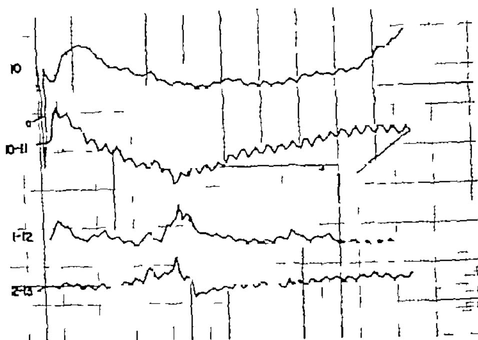


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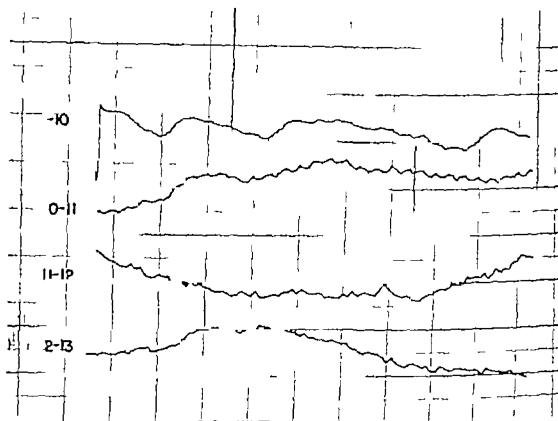


Fig. 1a

Bilateral ablation of the labyrinths or of the second somatic sensory area

Following bilateral labyrinthectomy the onset of rotation failed to induce cortical responses (Figs 4 and 4 *a*)

The possibility had to be investigated whether a spread of current or conduction of impulses from the second somatic sensory area to posterior parts of the hemisphere may have caused the appearance of potential changes in the latter Therefore the rotations were repeated following uni or bilateral extensive lesions or ablations of the gyrus ectosylvius anterior and gyrus suprasylvius anterior Such lesions, however did not prevent the appearance of the above described evoked responses in posterior parts of the hemisphere (Figs 5 and 5 *a*)

DISCUSSION

It seems necessary first to discuss whether the evoked responses recorded at the onset of angular acceleration should be considered as short latency responses. For the somatosensory cortex of the cat, latencies varying between 8 and 14 msec (Hirsch *et al.*, 1961) were reported for the hand area of the human cortex peak latencies of 18 to 25 msec were measured by Kelly *et al* (1963) similarly Larson *et al* (1966) found for the first por

Fig. 5a. Averaged response to onset of 10 counterclockwise rotations 1 hour after the ablations shown in Fig 5. The electrode positions correspond to the posterior row marked by ink dot in Fig 5.

tion of the response[1] latencies of 15 to 20 msec on stimulation of the nervus medianus in man. On application of sound stimuli Rapin (1964) found the first peak 5–12 msec after the click, while Davis (1964) designated responses to clicks of less than 50 msec to the highest peak as "fast". In a micro-electrode study of the cortical responses to labyrinthine stimulation by

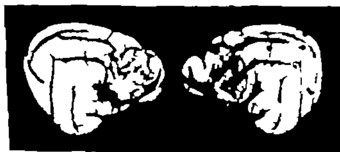


Fig. 5. Bilateral ablation of the gyrus ecto- and suprasylvius anterior.

[1] The latencies measured from the stimulus to the peak of the responses, of course are a few msec longer than those measured from the stimulus to the beginning of the response.

polarization Kornhuber & Fonseca (1964) distinguished specific primary cortical responses with short latencies of 5 to 30 msec and specific associative responses with latencies of 25 to 150 msec

If one accepts the classification according to the latency of the responses,[1] our observations would indicate that the starting of angular acceleration may elicit not only in the second somatic sensory area but also in posterior parts of the hemisphere specific primary as well as specific associative responses We do not have sufficient data to make definite statements regarding the effect of the onset of angular acceleration upon the primary somatic sensory area

On electric stimulation of the vestibular nerve and recording with macroelectrodes Mickle & Ades (1952 1954) failed to find evoked responses in the region of the gyrus ectosylvius posterior On polarization of the labyrinth however Grüsser *et al* (1959 1960) and Kornhuber & Fonseca (1964) using microelectrodes, recorded responses from the visual and paravisual regions These responses showed chiefly a long and variable latent period so that Kornhuber & Fonseca conclude that vestibular stimulation elicits only unspecific responses in the optic cortex and its vicinity Yet the experiments reported by Grüsser *et al* demonstrated that the discharge rate of cells of the visual cortex was influenced by vestibular impulses only while acoustic or trigeminal stimuli did not have such an effect These experiences seemed to indicate that a specific vestibular effect upon the optic cortex does exist Thus, while the latency measurements of unit discharges showed only unspecific responses of the optic cortex and the surrounding areas on labyrinthine polarization the comparison of the effectiveness of such a stimulation upon the discharge rate of the cells of the visual cortex with the negative effect of acoustic or trigeminal stimulation suggested the existence of specific vestibular effects upon the visual area Grusser *et al* attempted to meet this problem by assuming that afferent fibers with a specific function exist within the unspecific system. Similarly Jung (1961) believed that the functional significance of vestibulo-retinal convergence in the primary visual cortex is not only a nonspecific arousal but also a specific sensory regulation he considered the latter to be more important for sensory information but recognized that the long latencies of the cortical responses in the visual area present difficulties to the interpretation of specific functions of these vestibular cortical connections

These difficulties of explaining a specific labyrinthine effect upon the

[1] Other criteria, such as type of the starting of the reaction which can be studied on unit discharges relationship between the end of the stimulus and that of the response could not be applied in this study of the effect of acceleration upon cortical potentials with macroelectrodes. We are aware that between 50 and 250 msec there may be an overlapping of the latencies of specific associative and of unspecific responses (Kornhuber) However the major part of the latencies observed in the present study are below 50 msec

visual cortex no longer exist in view of the present finding that vestibular stimulation by angular acceleration may induce at least in some of the cats studied, also responses with a relatively short latency in the vicinity of the visual cortex. In this connection old experiments of one of us (Spiegel 1932) may be mentioned in which, following strychninization of the region of the gyrus ectosylvius posterior labyrinthine stimulation by rotation induced epileptiform convulsions.

For an explanation of the differences of the results obtained by Grüsser et al. (1959, 1960) and by Kornhuber & Fonseca (1964) and in the present experiments regarding the latent periods of the responses appearing in the posterior part of the hemisphere, it may be pointed out that Grüsser as well as Kornhuber could only use very weak currents for polarization of the labyrinth, because they obtained with stronger currents stimulation of other nerves (cochlearis, intermedius). Furthermore in their experiments the labyrinth of one side only was stimulated while rotation produces an endolymph flow in both labyrinths. As to experiments with macroelectrodes one has to remember that the use of the averaging technique permits one to demonstrate responses that may be masked by the background activity of the cortex.

ZUSAMMENFASSUNG

Unter Benützung eines Mnemotron-Computers wurde eine Methode entwickelt, die es gestattet, bei Katzen die Rindenreaktionen im Beginn von Drehungen zu studieren. Mit Hilfe dieser Methode konnte bestätigt werden, dass labyrinthäre Impulse in die zweite somatische sensorische Region (S_2) eintreten. Es wurde aber gefunden, dass die Rindenprojektion dieser Impulse nicht auf S_2 beschränkt ist, sondern weiter nach rückwärts reicht, hauptsächlich in Teile der Hörrinde und die sogenannte Assoziationsrinde (Gyrus suprasylvius medius). Zumindest in einigen Versuchen zeigten der vordere Teil des Gyrus ectosylvius posterior und die hintere Ecke des Gyrus suprasylvius medius (Teil der zweiten Sehregion) Reaktionen von relativ kurzer Latenz. Allgemeinlähmung oder beiderseitige Abtragung von S_2 verhinderten nicht das Auftreten solcher Reaktionen im hinteren Teile der Hemisphäre während beiderseitige Labyrinthausschaltung sie beseitigt.

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OBJECTIVE TINNITUS OF THE VASCULAR TYPE

A Follow-up Study

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Twenty-four patients with objective tinnitus of the vascular type were included in a follow-up study at the end of 2–15 years. This form of tinnitus may be divided into 2 groups (1) Tinnitus caused by anomaly within the arteries of the head or neck, (2) so-called essential objective tinnitus whose cause is presumably to be searched within the venous return from the head. The poorest prognosis was found in the patient of group 1 In cases where the diagnosis, in respect to the accurate location of the disease was uncertain, exploratory operation proved at best ineffective and in one case entailed severe complications. In the essential type the prognosis was quite favourable the tinnitus subsiding spontaneously in 7 of the 13 patients within a few weeks up to 3 years. In 3 of the remaining patients the tinnitus was reported to persist after the course of several years, but it was no longer felt to be bothersome The author advances the hypothesis that the essential type of tinnitus is due to abnormalities of the bulb of the internal jugular vein

Objective tinnitus, unlike subjective (or intrinsic) tinnitus, may be perceived not only by the patient, but also by the examiner on auscultation of the auditory canal and/or the neighbouring structures As the causes of objective tinnitus Atkinson (1947) mentioned (a) vascular bruits, (b) muscle spasms, (c) nasopharyngeal sounds, and (d) "clicking jaw" Among these types the one of vascular origin makes up the largest group and also occupies a special position, being greatly harassing to the patient There have even been reports of suicide for this reason

This type is a rare condition According to Graf (1952) only 50 cases were on record up to 1952.

In the University Department of Otolaryngology Copenhagen 24 patients with objective tinnitus of the vascular type were seen during the period 1951–1966 It is our general impression that the spontaneous course is more favourable than generally assumed. As there have been no systematic analyses of the course we have carried out a follow-up study of all our patients.

Vascular tinnitus may be divided into 2 groups One group, which may be called type A in which angiography has shown the tinnitus to be due to anomaly within the arterial system in the head or neck (arterial

aneurysm angioma racemosum arterial stenoses) and another group in which the cause has to be searched within the venous return from the head. This group which Graf (1952) named essential tinnitus, we shall call type B There remains a small number of cases in which the cause of tinnitus is presumably also vascular only this cannot be diagnosed by angiography In the present analysis such cases will be assigned to type A.

Essential Objective Tinnitus

According to Graf the essential type is characterized by fairly uniform symptoms *and signs and by the fact that it is impossible to demonstrate its cause*

Various factors indicate that the cause is to be searched within the venous system of the head or neck A very light pressure upon the neck or an alteration in the position of the head may make the sound disappear The pressure required is so light that it cannot possibly amount to arterial compression As a rule turning of the head towards the affected side (negative sternocleid position, Much (1912)) will lessen or check the noise while turning to the opposite side (positive sternocleid position) has an aggravating influence or none In practically its entire course the internal jugular vein runs immediately deep to the sternocleidomastoid muscle and it was clearly demonstrated by Much that turning of the head towards one side arrests or reduces the venous return from the homolateral part of the brain causing a correspondingly greater flow through the contralateral internal jugular vein According to Much the explanation is presumably that the internal jugular vein on one side gets squeezed behind the sternocleidomastoid muscle while on the opposite side it is kept dilated like a patent tube behind the contracted sternocleidomastoid muscle so that the flow to the central veins is improved

Essential tinnitus is nearly always—like arterial tinnitus—synchronous with the pulse since as is well-known there is distinct pulsation in the intracranial venous system as well as in the adjacent part of the extracranial venous return

Graf set up the following criteria for calling objective tinnitus essential

(1) Sudden onset unrelated to other diseases or injury (2) persistence unchanged for more than one year (3) definite objective tinnitus, (4) pronounced *lateralization (5) synchronicity with the pulse (6) certain relations to alterations in head position* (7) no symptoms of increased intracranial pressure (8) no pulsating exophthalmos, (9) no abnormalities of extracranial arteries, (10) a normal cerebral angiogram

In the analysis of our material it was found that according to the named criteria *the patients could be naturally divided into one* group of essential tinnitus (type B) and another group having tinnitus of other causes (type A)

MATERIAL

The material comprised 24 patients, 18 women and 6 men The women ranged in age from 16 to 82 average 46 6 years while the men were from 35 to 55 years, average 46 3 years All were seen in the University Department of Otolaryngology during the period 1951–1966 In one case the

follow-up period was only 18 months, while for the others it was 2–15 years, average 7 7 years.

All the patients had subjective tinnitus, synchronous with the pulse and demonstrable objectively by auscultation in one or more sites on the skull and/or with an otoscope tube in the auditory meatus.

In a number of the patients the tinnitus had been recorded electrooscillographically by means of a phonocardiograph Two of these cases have been published previously (Davidsen & Thomsen 1956) The tinnitus could be recorded in relation to the heart beat and was found to have its maximum invariably at the time of systole. This applied to patients with type A as well as with type B tinnitus. Thus, the method is of no value in ascertaining th cause of the tinnitus. Engström & Graf (1952) arrived at the same result by a similar method

In 13 cases the tinnitus fulfilled Graf's criteria as being essential, i.e. presumably due to an an maly within the venou system in the head or neck

Among the remaining 11 cases, the cause of the tinnitus was found in 7 while in 4 cases it was not possible to detect any explanation. In these 4 patients the tinnitus did not fulfill the criteria for being classified as essential

Case Reports Objective Findings Operations if any and Diagnosis

The 13 patients with essential tinnitus may reasonably be considered together Two were males and 11 females. Average age 39 years (16–64 years) In all cases the onset had been spontaneous In 12 of the patients the tinnitu could be checked by turning the head and/or by exerting pressure upon the neck so light that it could not cause arterial compression In 3 of th 12 cases (Cases 2, 4 and 6 in Table 1) the tinnitus did not yield until the internal jugular vein was clamped during peration (clamping of the xternal carotid artery the internal carotid, or the occipital artery had first been tried ineffectively) In one of the 13 cases the effect of venous compression or turning of the head had not been studied, but the history the normal carotid and vertebral angiography as well as the course made it reasonable to place the patient in this group

All 13 patients h d been subjected to angiography of the carotid artery (3 of the patient twice) Three had, in addition, had angiography of the vertebral artery In 12 cases th angiograms were normal. In one there was narrowing of the internal carotid artery on th homolateral side but as there wa the bove-mentioned effect of positive and negative sternoeld position a well as of enous compression, the patient was included in th essential group.

In one case otoscopy revealed the sequela of otitis, while in the others the drum were normal In particular none of these patients had bluish or pulsating areas on the drums.

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MATERIAL

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Case sex, age	Onset of tinnitus	Length of history (years)	Type	Diagnosis	Surgical procedures	Course	Observation period (years)
17 F 35	Suddenly following hyperemesis	1	A	Arterio- eno- us nasto- mosis of the neck	Ligature of ana- tomosis in tw tages, see t xt	Hemiparesis following operation Tinnitus unchanged	12*
18 F 42	Suddenly follo ing fatiguing walk	½	A	Arterio- eno- sus aneurysm of the neck?	0	Unchanged not nnoying	1½
19 M 55	Suddenly following otitis media	15	A	Objective tinnitus	Ligature of the homolateral occi- pital artery	Disappeared after operation. Recurrence 24 hours later Aggravated	7*
20 F 44	Spontaneously suddenly	½	A	Racemous angioma of the neck	Excision of angioma	Disappeared after operation	7*
21 M 54	Spontaneously	1	A	Atheroma of internal ca- rotid artery	Removal of theroma	Disappeared after operation	5
22 M 33	Spontaneously	½	A	Objective tinnitus	0	Disappeared after a-graphy	6
23 F 61	Spontaneously	1a	A	Objective tinnitus	0	Tinnitus ggravated	9*
24 M 46	Following physical exercise	1/12	A	Stricture f the internal carotid artery	0	Disappeared fter few months	5

Patients answered questionnaire and were not examined.

Operation

Three of the 13 patients had ligation of the internal jugular vein and one ligation of the external carotid artery

Cases 11 12, and 13 will be reported in some detail below

Case 11 ♀ aged 19

T t rose after sy nging th ear d had been present for one yea Duri g the same period impaired visio d obscurations. Opthalmological am nation revealed hoked discs +3.3 +4 diopires. EEG Slightly t moderat ly abn rmal. Carotid ngiography \ bnorm l ly The diagnosi wa essential t nitus, ntracra ial hyperten ion f unknown cause d basal arach iditis.

Case 12 ♀ aged 40

Th reason why thi p tient w admitted was that because f the tinnitus she had been subjected, i nother hospital, t ca otid giography which had been followed in a few hours, by h m lateral hemiparesi The ti nitus disappeared for 2 week after th angiography Then f llowed mild recurr nce which did ot bother the p tient. Four years later he still had objective tinnit of the essential type

TABLE 1

Case sex, age	Onset of tinnitus	Length of history (years)	Type	Diagnosis	Surgical procedures	Course
1 M 35	Spontaneously gradually	½	B	Essential tinnitus	0	Disappeared spontaneously after 3–4 years
2 F 26	Spontaneously	1	B	Essential tinnitus	Ligature of the homolateral internal jugular vein	Tinnitus reduced after operation, disappeared after a few months
3 F 16	Spontaneously	¼	B	Essential tinnitus	0	Disappeared after a-graphy
4 F 22	A few months after minor fracture of base of skull	5	B	Essential tinnitus	Ligature of the homolateral internal jugular vein	Disappeared after operation. Recurrence after a few days. Disappeared about one year later
5 F 41	Spontaneously	¼	B	Essential tinnitus	0	Disappeared spontaneously after 10 years
6 F 24	Spontaneously gradually	3½	B	Essential tinnitus	Ligature of the homolateral internal jugular vein	Disappeared after operation. Recurrence after 24 hours. Disappeared after 37 chiropractic treatments
7 F 52	Suddenly in the course of influenza	1	B	Essential tinnitus	0	Tinnitus unchanged, not annoying
8 F 34	Spontaneously gradually	1	B	Essential tinnitus	0	Disappeared after a-graphy. Recurrence after 1 month. Disappeared after 1 chiropractic treatment
9 F 64	Spontaneously gradually	¼	B	Essential tinnitus	0	Disappeared after a few weeks. A persisting white noise was not annoying
10 M 49	Spontaneously	¾	B	Essential tinnitus	0	Disappeared after 1 year
11 F 49	Suddenly following irrigation of the ear	1	B	Essential tinnitus, see text	0	Tinnitus unchanged, not annoying
12 F 40	Spontaneously	1½	B	Essential tinnitus, see text	0	Hemiparesis following a-graphy, see text
13 F 46	Spontaneously gradually	1	B	Essential tinnitus, see text	Ligature of the homolateral ext. carotid artery	Complicated with hemiparesis, see text
14 M 50	Suddenly following head injury	¼	A	Fistula caroticocavernosa	Partial ligature of the homolateral common carotid artery	Disappeared after operation
15 F 61	Spontaneously gradually		A	Objective tinnitus	Ligature of the posterior auricular artery	Disappeared after operation. Recurrence after a few days. Disappeared one year later following appendectomia
16 F 70	Spontaneously	¼	A	Arterial hypertension	0	Disappeared after 2 years

operation. In one case with definitely diagnosed vascular anomaly (Case 1) the anomaly was corrected, but the tinnitus persisted unchanged, and the operation was complicated by hemiparesis. (This was a technically very difficult operation) In another case of definitely diagnosed vascular anomaly (Case 24) operation was advised against, and the tinnitus subsided spontaneously after having been present for many years. In yet another case the tinnitus was presumably due to vascular anomaly (extracranial arterio-venous anastomosis, Case 18) but owing to advanced age and the slight subjective complaints no operation was offered.

In 2 of the remaining 5 patients in this group (Cases 15 and 22) the tinnitus was presumably of the essential type (spontaneous onset, normal angiography disappeared after minor procedures) No explanation of the tinnitus was found in 3 cases. In one it disappeared spontaneously (possibly it was due to hypertension Case 16) while in the other two (Cases 19 and 23) the prognosis has been very poor the tinnitus still being extremely uncomfortable 7 and 9 years later

DISCUSSION AND CONCLUSION

W agree with Graf that the so-called essential type of objective tinnitus is clearly distinguished in this motley group of patients by its ymptom as well as its course

In Engström & Graf's series (1952) 6 out of 12 cases of objective tinnitus were of the essential type In the present material this ratio is identical (13 out of 24)

In all series of objective tinnitus the sex ratio has been ♀/♂=2–4/1 (Hamburger 1931 Igl uer 1933 Sears, 1938 Dalsgaard-Nielsen, 1939 Graf 1952 Graf *et al* 1947 Atkinson, 1917 Engström & Graf 1950) Our material comprised 6 males nd 18 females. The marked female preponderance ppears to apply especially to the essential group in which 11 out f 13 were females, while in the remaining part of the material 7 out f 11 were f males

According to Graf th age of predilection for essential tinnitus is 20–40 years, and it is said that aft r the age f 65 it does not occur The average g n our material wa 39 years (16–64 years) In this respect too, it is in keeping with Graf's findings.

Th first idea that enters one s head when faced with a case of objective tin tus i vascular anomaly Strangely enough only a few vascular nomalies in the head and neck give rise to objective tinnitus. Thus, Bergstrand *et l* (1936) found thi phenomenon in only 4 out of 22 cases of intracranial aneurysms and in 1 out of 13 cases of angioma racemosum. Dalsgaard Nielsen (1939) found objecti tinnitus in 2 out of 7 cases of rterio-venous aneurysms.

Angiography is an important diagnostic procedu e but venous compres ion i just as important, wh th it is done manually (possibly after ex

Case 13 ♀ aged 46

Previously published by Arnvig (1953)

In this patient the tinnitus disappeared upon light pressure on the neck upon turning the head to the right but was erroneously interpreted as being of arterial aetiology The patient was therefore transferred to another department, and the homolateral external carotid was ligated but a few hours later contralateral hemiparesis occurred The next day reoperation was performed loosening the ligature After the first operation and before the ligature was loosened the patient reported that the tinnitus was unchanged After the ligature had been loosened the tinnitus disappeared Four weeks later it recurred but was no longer so annoying Fifteen years later there was no objective tinnitus. The hemiparesis subsided in 9 months.

The remaining 11 patients with vascular tinnitus of type A

The case data are given in Table 1

Only Case 17 will be reported in more detail In this woman aged 35 the tinnitus had arisen during hyperemesis of pregnancy She had left sided tinnitus and a soft, heavily pulsating mass behind the left mastoid process. The tinnitus disappeared when the left common carotid was compressed Carotid angiography showed that possibly there was an anastomosis between a neck vein and the internal carotid artery An exploratory operation on the neck was done ligating an enlarged occipital artery and numerous tortuous veins in the vicinity The tinnitus disappeared but returned with increased severity 24 hours later The pulsating mass behind the mastoid process had disappeared but repeated angiography revealed that there was still a deep-lying arterio-venous anastomosis in the neck. The patient was transferred to another department and at re-operation an anastomosis between the posterior meningeal vein and the internal and external carotid arteries was ligated Postoperatively she developed retrograde thrombosis of the internal carotid artery with hemiplegia and aphasia The tinnitus remained unchanged and 12 years later there was still paresis of the arm, and the tinnitus was said to be still very severe

Course (Table 1)

I 13 patients with essential tinnitus

1 In 5 patients the tinnitus disappeared spontaneously (at the end of a few weeks 1 1 3 and 10 years)

2 In 6 patients the tinnitus yielded to minor procedures (angiography manipulations) However 3 had recurrences

3 4 patients had operations In 3 it consisted in ligation of the homolateral internal jugular vein Only one of the patients benefited permanently The 4th operated patient was described above (Case 13)

4 In 3 cases the tinnitus remained unchanged at the end of 3 8 and 10 years, but the patients reported that it was not annoying

II 11 patients with vascular tinnitus of type A

The individual data are given in Table 1 Case 17 was reported above

Summing up this group it may be said that in 3 patients with definitely diagnosed vascular anomalies (Cases 1 20 and 21) the tinnitus yielded to

of Otolaryngology Copenhagen, seem to indicate that essential tinnitus is due to anomalies of the bulb of the internal jugular vein By means of retrograde jugularography supplemented by tomography attempts are being made at confirming this assumption. To the author's knowledge no such studies have previously been performed on patients with essential tinnitus.

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posure of the vascular sheath) or by placing *the head in the negative* sternocleid position (*vide supra*)

In many normal persons slight changes in the impedance of the drum, synchronous with the pulse no doubt occur because of pulsation of the vessels in the middle ear By impedance measurement it ought to be possible to ascertain whether the vascular phenomena which condition tinnitus are accompanied by an abnormally heavy pulsation in the middle-ear vessels In unilateral cases, there ought to be particularly good possibilities of assessment by comparing with the other normal ear It was not possible *to demonstrate any abnormal degree of pulsation in any of our* *t* patients who had such impedance measurement Two of these cases have previously been published by Davidsen & Thomsen (1965)

The present analysis was carried out largely to ascertain the prognostic outlook It is clearly evident that patients with tinnitus of the essential type had a more favourable prognosis In 10 of the 13 cases the tinnitus has disappeared, although in some of the cases it did persist for a long time The 3 patients who still had tinnitus at follow up reported that they were not much bothered by it Two of these 3 patients have sent written replies *to inquires while the 3rd patient was examined, but the tinnitus could* not be demonstrated objectively

Out of the remaining 11 patients 4 had operations for definitely diagnosed vascular anomalies In 3 cases the operations resulted in relief of symptoms. In one case, however the operation proved extremely difficult and was complicated by hemiplegia the tinnitus remained unchanged

Among the 4 patients whose diagnosis was uncertain because no cause of the tinnitus could be *found* and the patients *did not fulfill the criteria* of the essential type, there were the 2 patients who had the poorest prognosis, as they still suffered *from severe* tinnitus at the end of 7 and 9 years In the other 2 the tinnitus disappeared in the course of a couple of years Thus, in spite of the findings, it might be presumed that the genesis was the same as in the essential type

As far as the treatment of objective tinnitus is concerned our results show that operation should not be attempted *unless there is a definitely* diagnosed vascular anomaly In cases where the diagnosis in respect to *vascular anomalies* was *less* certain operations were at best ineffective (Cases 15 and 19) and at worst entailed serious complications (Case 13)

The logical treatment of essential tinnitus, in cases where compression of the internal jugular vein immediately stops the noise, is ligation of this vein Indeed this had been tried in 3 of the 13 patients with essential objective tinnitus but a lasting *effect* was obtained *in only one In the* other 2 the tinnitus disappeared entirely after the ligation but returned in *a few days Graf* also found recurrence shortly after ligation of the internal jugular vein In his opinion the explanation is that collaterals develop in a short time Instead he suggested obliteration of the sigmoid sinus

Investigations which have been instituted in the University *Department*

of Otolaryngology Copenhagen, seem to indicate that essential tinnitus is due to anomalies of the bulb of the internal jugular vein. By means of retrograde jugularography supplemented by tomography attempts are being made at confirming this assumption To the author's knowledge no such studies have previously been performed on patients with essential tinnitus.

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DISTRIBUTION OF EFFERENT NERVE ENDINGS IN THE ORGAN OF CORTI

Their Graphic Reconstruction in Cochleae by Localization of Acetylcholinesterase Activity

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The efferent innervation of the organ of Corti was studied in normal cats The efferent nerve endings were visualized in serial frozen sections by demonstrating specific AChE activity in them Innervation of the outer hair cells gradually decreased in the apical direction to the point where no efferent innervation was present this was more evident in the outer row than in the inner row of outer hair cells. AChE activity was poorly visualized around the inner hair cells, but was very strong in the inner spiral bundle of nerve fibers throughout the cochlea These observations are in agreement with pertinent electron microscopic and electrophysiological data

The efferent feed-back" system to the inner ear originally described as the olivocochlear bundle by Rasmussen in 1946 has been widely studied with anatomical and physiological methods Churchill *et al* (1956) histochemically demonstrated that the efferent system of the organ of Corti has marked acetylcholinesterase (AChE) activity While this characteristic of the efferent system has been used to trace the course of the nerve fibers in various species (Rossi 1961 Hilding & Wersäll 1962 Smith & Rasmussen 1963 Spoendlin & Gacek 1963 Gacek *et al* 1965 Nomura & Schuknecht 1965 Ishii *et al* 1967) little is known about the distribution of the nerve endings Although electron microscopic studies have shown differences in the type and distribution of nerve endings in the cochlea relatively fewer hair cells have been investigated because of the limitations inherent in electron microscopic techniques. Thousands of hair cells can be examined with the light microscope if the nerve endings are visualized with the zinc iodide technique of Maillet (Engström *et al* 1966) Since high AChE activity in the inner ear appears to be limited to the efferent nervous system,

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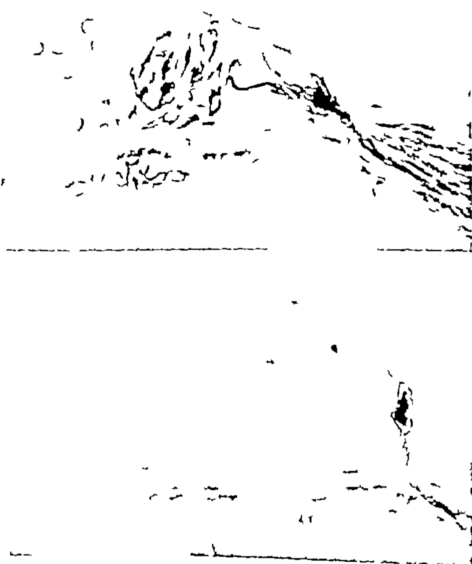


FIG. 1 Phase contrast microscopic iew of the organ of Corti. AChE activit is localized histochemically t the efferent nerv fibers and nerv endings which ppear black on the photographs. (A) About 10 mm from the basal end, the first nd second rows of outer hair cells show nerve nerv endings, but the third row ha only parse inner tion. This pattern has been l ssified as 331 in the graphic reconstruction nd diagram. (B) Efferent nerv tion is not demonstrable in the outer hai cells nea the pical end. This w evaluated as 000 i the diagram. Notice the abundant AChE activity in the i ner piral bundle

the histochemical approach is highly specific for the demonstration of efferent innervation Utilizing the histochemical technique it was possible to study the distribution of the efferent nerve endings in the cat. The present paper reports the results of this investigation

MATERIALS AND METHODS

Five normal cats, weighing 3000–3600 g, were anesthetized by intraperitoneal injection of 50–100 mg/kg pentobarbital sodium The animals were perfused through the left cardiac ventricle with 300 cc of Ringer's solution followed by 300 cc of cold 4° neutral formol-calcium They were then immediately decapitated and their temporal bones were removed. The inner ears were trimmed as small as possible and fixed overnight at 4 C in 4% neutral formol-calcium. The bones were decalcified with a 10% buffered solution of cold EDTA for 30–40 days (Balogh & Nomura 1964) The decalcified bones were frozen on dry ice and cut serially with a rotary microtome in a cryostat (−30 C) at 10 μ Every tenth section was incubated for 40–60 minutes at 37 C to localize AChE activity using Koelle's method as modified by Gomori (Gomori, 1952) Cell nuclei were counterstained with methyl green

Various enzyme inhibitors were employed to check the specificity of the histochemical reaction. Eserine salicylate (in a final concentration of 10^{-4} M) was used as an inhibitor for both AChE and cholinesterase (ChE) activity Silver nitrate (in a final concentration of 10^{-4} M) and OMPA (octamethylpyrophosphoramide, in a final concentration of 10^{-} to 10^{-3} M) were used for the inhibition of ChE. Butyrylthiocholine iodide was used as a substrate instead of acetylthiocholine iodide to demonstrate ChE activity

After studying the sections with the light or phase contrast microscope, graphic reconstruction of each organ of Corti (Schuknecht, 1953) was made to demonstrate the distribution pattern of the efferent nerve endings for the entire length of the cochlea Obviously the experimental conditions influence the amount of copper sulfide deposited at the sites of AChE activity Individual nerve endings were frequently discernible, nevertheless the extent of innervation was evaluated by the area of the histochemical reaction rather than by its intensity The observations made on each cross section of the organ of Corti were arbitrarily graded on 0 to 3 plus scale depending upon the area occupied by the nerve endings. Thus, the extent of innervation of the outer hair cells could be expressed as a number the first digit indicating the innervation of the innermost outer hair cell e.g. 331 (Fig. 1 A) 000 (Fig. 1 B) etc.

RESULTS

The distribution of the efferent nerve endings was similar in all temporal bones. A typical example is shown in Figs. 2 and 3 In the basal turn the first

OUTER HAIR CELL

1st Row



2nd Row



3rd Row



Fig. 2. Diagram f efferent i nervation of the normal cochlea (the same nimal as i F g 1). Notice the decrease f efferent nerv endings toward the pex, especially in the third row of outer hair cells.

enzyme activity in th hairs of sensory cells as well as other obvious arti facts in the microphotographs lea e serious doubts about the validity of their results. Recently Mounier Kuhn & Haguenauer (1967) have also uti lized flat preparations for the histochemical demonstration of AChE activity in normal and cou tically stimulated guinea pigs. They found diminished enzyme ctivity in the oute row of hair cells; this was thought to be the result of acoustic stimulation. However diminution of AChE activity in the outer row f hair cells was seen in all our normal animals, too. The obser ati ns made in the present study can be correlated, therefore, only with pertinent electron microscopic and physiological data.

Unde the electr n microscope Engström (1958) observed in the guinea pig granulated and non-granulated types of nerve endings around the oute hair cells. He observed that granulated nerve endings were abundant in the inner row f outer hair cells but were less numerous towards the outer row. Smith & Sjöstrand (1961) have studied with the electron micro-scope serial sections f outer h ir cells. They found two types of oute h ir cell one that is equally well innervated by both the efferent and afferent nerves. The second cell type which is m re numerous in the apical area, ha less fferent nerve endings. The efferent nature of the granulated nerve ending has been proven experimentally after transection of the ll oecochlear bundle they degenerated, whereas the non-granulated nerve ending remained normal (Kimura & Wersäll, 1962 Bairati & Iurato, 1962)

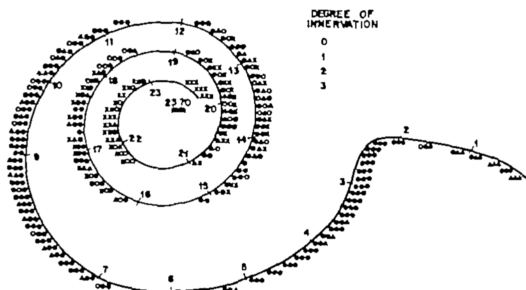


Fig 2 Graphi recon tructio f efferent nerve nding n outer hair cell in a norm l cat Inner ati n wa graded arbitrarily on a 0 to 3 plus scale by evalu ting the extent f hi toch mical reaction

row of the outer hair cells had numerous nerve endings, but in the apical region the area occupied by nerve endings diminished fairly abruptly The second row of outer hair cells showed a more gradual diminution of nerve endings towards the apex, beginning 10–15 mm from the basal end The third row of outer hair cells was the least innervated and innervation had already begun to diminish 5–10 mm above the basal end

Briefly efferent innervation was decreasing towards the apex, and this was more evident in the outer row than in the inner row (Fig 1 A) Near the apical end all three rows of outer hair cells lacked demonstrable efferent innervation (Fig 1 B) Another area of poor efferent innervation was consistently seen at the extreme basal end of the organ of Corti

AChE activity was poorly localized around the inner hair cells, but was very strong in the inner spiral bundle of nerve fibers throughout all turns of the cochlea (Fig 1 B)

DISCUSSION

Experiments with the enzyme inhibitors indicated that the efferent fibers and nerve endings contain only AChE activity whereas non specific ChE activity was noticed in other parts of the cochlea such as the stria vascularis, part of limbus spiralis and endothelial cells of blood vessels These data confirm pre i us observations that indicate the presence of specific AChE activity in the efferent nervous system of the inner ear (Churchill *et al* 1956 Ishii *et al* 1967)

Although Vinnikov & Titova (1958) claim to have demonstrated AChE activity in flat preparations of the organ of Corti their description of strong

es nicht möglich in den drei Reihen von äusseren Haarzellen eine Innervation nachzuweisen. Um die inneren Haarzellen war die Enzymaktivität kaum darzu stell n, hingegen w r sie im inneren Spiralbündel der Nervenfasern in der ganzen Cochlea stark ausgeprägt. Diese Beobachtungen stehen im Einklang mit den bekannten lektronen ptischen und neurophysiologischen Ergebni en.

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It is evident from recent electron microscopic observations in guinea pigs (Kimura) that one outer hair cell can have as many as five or six efferent endings while others may have fewer or none Similar observations were also made in the cat (Spoendlin & Gacek 1963) All these data correlate well with our histochemical results in cats

The inner hair cells presented some interesting problems in this study because satisfactory localization of AChE activity could not be observed at their base Likewise, Kaneko & Daly (1968) have been unable to demonstrate AChE activity in the nerve endings around the inner hair cells with the electron microscope using Karnovsky's method (1964) According to them some of the afferent nerve fibers do form synapse-like structures around the efferent inner spiral bundle Furthermore they could localize AChE activity on the surface of these synapse-like structures. Smith (1961) identified two types of nerve endings also at the inner hair cells, which she thought to be of an efferent type She noted however that more efferent fibers seemed to have contact with the afferent dendrites beneath the inner hair cell than directly reach the hair cell Such an unusual innervation would explain the negative histochemical reaction at the level of the inner hair cells In agreement with previous observations (Ishii *et al* 1967) the inner spiral bundle always revealed strong AChE activity

It has been widely accepted since Galambos original physiological study (1956) that the efferent innervation can inhibit the sound-evoked action potentials of the afferent auditory nerve fibers. These can be suppressed when the crossed olivocochlear bundle is stimulated electrically at the floor of the fourth ventricle of the brain (Galambos 1956 Wiederhold 1967) Recently this suppression of action potentials was found to be less effective for afferent fibers having characteristic frequency in the low and very high range than for those in the medium to high range (Wiederhold 1967) Our observations of reduction in innervation toward the apex and at the extreme basal end of the outer hair cells by the efferent system provide a qualitative anatomical explanation for these electrophysiological data

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ZUSAMMENFASSUNG

Die Verfasser berichten über die efferente Innervation des Cortischen Organs in normalen Katzen Die efferenten Nervendigungen wurden an Serienfefrierschnitten durch die histochemische Reaktion für Azetylcholinesterase dargestellt Es ergab sich dass die efferente Innervation der äusseren Haarzellen apikalwärt abnimmt diese Verminderung war in der äusseren Reihe mehr ausgeprägt als in der inneren Reihe der äusseren Haarzellen In der Nähe von der Apex war

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THE ROLE OF THE EUSTACHIAN TUBE IN MYRINGOPLASTY

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The importance of tubal function in the results of myringoplastic operation has been estimated in 72 cases with central ear drum defects as residues after chronic otitis media. The tubal function has been tested pre-operatively with the "aspiration method". More than one year post operatively the patients have been reviewed when hearing and healing were noted. The results were correlated to pre-operative tubal function testing results. In the group with "good" tubal function there was 75% healing and only 16% of the patients had perforations. In the "hypo-function" group almost 90% failed. Many factors besides the tubal function influence healing in myringoplasty. However the aspiration method for testing the Eustachian tube, according to this report, is able to give valuable prognostic information.

Success in hearing improvement surgery depends on many *factors*. *One* of the most important is an adequate function of the Eustachian *tube*. Tubal dysfunction is often responsible for many failures in tympanoplastic procedures (Zöllner 1963, Wullstein, 1963, *Farrior* 1965, Schuknecht & Kerr 1967). For this reason *tubal function* is always carefully checked in all patients with tympanic membrane or middle *ear defects before* reconstructive middle ear surgery. It is of great interest if a quantitative tubal function test can give *prognostic information* about tympanoplastic surgery.

There are only a few reports where the *pre-operative tubal testing* result in tympanoplastic surgery have been correlated to success or failure. The *reason for this might be that* the possibilities of a quantitative testing of the Eustachian tube have been *limited* and unreliable. A new method has now been introduced, the "*aspiration method*" which makes it possible to get a more precise estimation of the tubal function (Flisberg *et al.*, 1963). This technique has been used in the *present investigation*.

Technique of tubal testing according to the "aspiration method"

The testing procedure is shown in Fig. 1. A patient with a tympanic membrane defect is placed in a sitting position. The external auditory canal is

Based on a paper read before the Swedish Otolaryngological Society on December 2, 1967.

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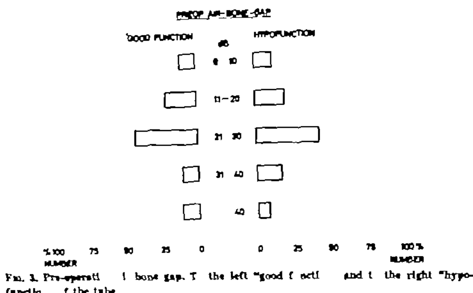


Fig. 3. Pre-operati l bone gap. T the left "good f ncti and t the right "hypo-functio f the tube

underpressure in the middle ear cavity. The procedure is continued until further deglutitions produce no further drops in the pressure. The testing is then finished and the remaining negative pressure in the middle ear which the patient is unable to reduce is called the "residual pressure". In this report we have used the residual pressure as an indication of the patient's tubal function.

After a preliminary pilot experiment we divided our tubal function testing results into two groups. "Good function" means that the patient is able to reduce the underpressure to a residual value in the range of 0–100 mm H_2O. "Hypofunction" means that the patient is unable to do that. The reality in

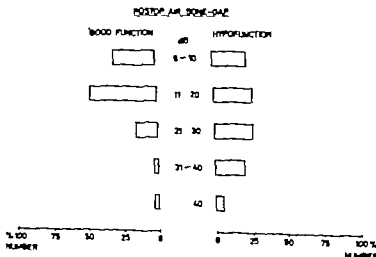


Fig. 4. Post-operati al -bone gap.

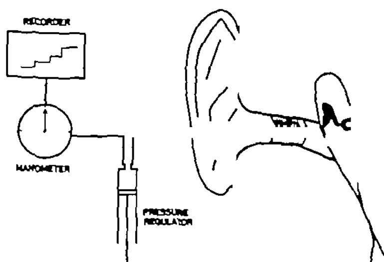


Fig 1 T sting procedure

connected to a pressure regulator a syringe and to a pressure transducer (Elema Schönander AB Stockholm Pressure Transducer EMT 490 B pressure range 0–30 mm Hg) The desired pressure is created in the middle ear cavity by the syringe The patient is then asked to swallow repeatedly If there are any pressure equalizations they are recorded (Minograf 34 Elema Schönander Stockholm) In the present report we have created an artificial

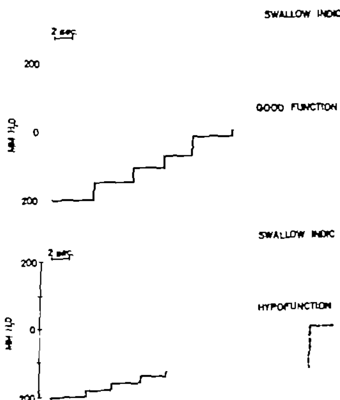


Fig 2. Recordings from 2 ases The upper half of the figure sh ws p ti t wh i abl to reduce − 200 mm H_2O to zero The lower half show pati t who i n abl to reduce the neg tive pres ure in the rang of 0 to — 100 mm H O

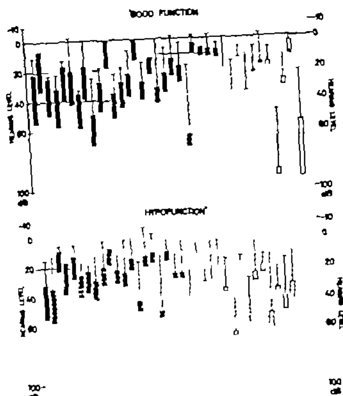


Fig. 4. Individual healing and hearing results. Unbroken lines and piles represent successful cases, interrupted lines and piles indicate post-operative perforation. Black columns indicate hearing improvement in dB. Empty columns indicate hearing impairment.

RESULTS

More than one year post-operatively the ear has been reviewed. The hearing has been estimated with pure tone audiogram and the healing examined in the Zeiss operation-microscope. With the aid of a Siegle's otoscope the mobility of the tympanic membrane has been observed.

For a number of reasons the hearing results are almost the same in the two groups. This is illustrated in Fig. 4 where the post-operative air-bone gap is shown. However the main factor we have analysed is the healing of the tympanic membrane. The results are shown in Fig. 5.

Satisfactory results have been obtained in 75% of the ears with "good" tubal function while only 12% of the ears with "poor" function healed. Post-operative perforation were noted in 16% of ears with good tubal function and in 0% of ears with "hypofunction". 3 cases with cholesteatoma included.

In Fig. 6 each case is shown separately. The unbroken lines and piles represent successful cases. The dotted lines and piles show post-operativ

HEALING RESULTS

GOOD FUNCTION HYPOFUNCTION

DRUMS WITHOUT OBJECTIONS

DRUMS WITH ADHESIONS

PERFORATIONS

CHOLESTEATOMAS

% 100 75 50 25 0 0 25 50 75 100 %

NUMBER NUMBER

Fig. 5. Healing results.

this partition has been tested in the present investigation. Fig. 2 illustrates "good function" and "hypofunction" of the tube. The upper half of the figure shows a patient with a central drum perforation and "good" tubal function. The patient is able to reduce the underpressure, in this case -200 H_2O, to zero. The lower half shows a patient with central drum perforation too, who is unable to reduce the pressure in the range of 0 to -100 mm H_2O.

Tubal function tested in this way gives reliable information about the Eustachian tube only at the moment of testing. However, if the same patient is tested repeatedly it is very uncommon to find great variations. In this investigation 40 out of 72 patients have been tested at least twice. In these results only 5% of the patients have a difference in the residual pressure exceeding 40 mm H_2O between two testings.

MATERIAL

The material consists of 72 patients, 31 men and 41 women, with residues after chronic otitis and with dry central ear drum perforations. The age range is from 8 to 72 years. Pre-operatively 37 had what we called "good function" and 35 "hypofunction" of the tube. From the hearing point of view there is no difference between the two groups, which is shown in Fig. 3 where the air bone gap is illustrated.

As far as possible a uniform operation procedure has been performed, all by endaural approach. When necessary we have explored the middle ear cavity. The tympanic remnant has been de-epithelialised. A graft from the fascia of the temporal muscle has been applied on to the drum remnant. The ear canal has been packed lightly with a gauze tamponade soaked in antibiotic-corticosteroid solution.

tion hatten annähernd 90% kein zufriedenstellend Heilung. Ausse der Tubenfunktion wird das Heilungsergebnis on ielen anderen Faktoren beeinflusst. Die Aspirationsmethode zur Prüfung der Tubenfunktion gibt jedoch laut diesem Bericht wertvolle prognostische Hi weise

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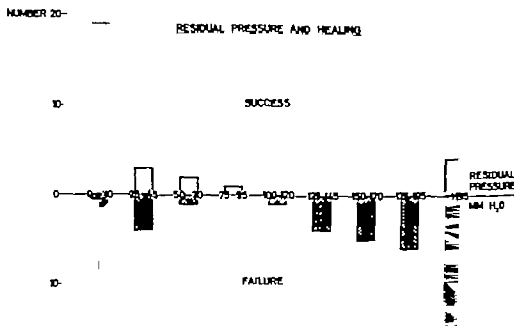


Fig. 7 Negati residual pressure correlated t h aling

perforations The black piles show the hearing improvement in dB The empty piles show the hearing impairment The figure shows among other things that only 4 of the ears with hypofunction" but 24 with good function healed with hearing improvement

DISCUSSION

In this investigation we have found good correlation between the healing results one year after myringoplastic operation and pre-operative "good tubal function i e the ability to reduce underpressure in the range of 0 to − 100 mm H_2O This is shown in Fig 7 With further experience regarding this method the limit value 100 mm H_2O may be changed It is interesting that 4 ears (12%) with impaired tubal function healed However it is plausible, at least in two of the cases, that the operative procedure has changed the tubal function

ZUSAMMENFASSUNG

Die Bedeutung der Tuba Eustachii bei Myringoplastik wurde in 2 Fällen mit zentralen Trommelfellperforationen gewertet Die Tubenfunktion i t präoperativ mittels der Aspirationsmethode geprüft worden Postoperativ wurden die Patienten über ein Jahr untersucht wobei das Gehör und die Heilung notiert wurden Die Ergebnisse wurden mit den präoperativen Tubenfunktionsergebnissen in Zusammenhang gebracht In der Gruppe mit „guter Tubenfunktion heilten und nur 10% der Patienten wiesen Perforation auf In der Gruppe Hypofunk

betrachten (Cenkovich & Gersten, 1963 Kaiser & Petersen, 1963) ferner den Versuch einer objektiven Registrierung von Fibrillationspotentialen durch einen Impulszähler mit einer auf 10 µV eingestellten Diskriminator spannung (Skorpil & Zverina, 1963) die Methode von Koepchen & Heinich (1964) zur fortlaufenden Registrierung von Aktionspotentialen und Aktionspotential Frequenzen mit mechanischen Direktschreibern sowie ältere Integratorschaltungen zur direkten Aufzeichnung von elektrischer Aktivität im EMG (Delhez *et al* 1964)

Da Potentialamplitude und Entladungsdichte zusammen in das Integral eingehen, ist dieses stark von der Position der Nadelelektrode abhängig und für die Analyse pathologischer Fälle oft unbrauchbar Interessant ist die elektronische Bestimmung des Zeitganges von Amplituden im H Reflex, entwickelt von Matsuoka u Mitarb (1966) für stereotaktische Operationen Diesen Versuchen steht eine hochgetriebene elektronische Analyse von Einzelableitungen aus dem Zentralnervensystem und des Elektroenzephalogramms gegenüber (z. B. das Symposium über Computer techniques in EEG-Analysis ferner Gerstein, 1961 Keidel, 1965 und 1967 Keidel & Spreng, 1965 Houk *et al.*, 1964 Simon, 1965 Boudreau, 1966)

Warum wurde die klassische Elektromyographie bisher nicht mit datenverarbeitenden Methoden erweitert? Das Hindernis liegt u a. in zwei Besonderheiten 1) Die übliche Ableitungselektrode sammelt die Entladungen verschiedener motorischer Einheiten, die daraus entstehenden Überlagerungen (Interferenz) verhindern oft ein direktes Auszählen von Potentialen, Entladungsfrequenzen und Amplituden. 2) Die mechanische Bewegung des aktivierten Muskels ruft oft eine Nullpunktsverschiebung hervor die den Analog Rechenvorgang empfindlich stört. Der Wunsch nach einer verbesserten Diagnostik peripherer Fazialislähmungen sollte jedoch die systematische Überprüfung aller in Betracht kommender EMG-Parameter ermutigen. Einer der wichtigsten ist die Dauer des Aktionspotentials der motorischen Einheit, weil sie bei Paresen erfahrungsgemäß verlängert ist Buchthal (1958) fand eine signifikante Zunahme in der Hälfte seiner Fälle Wir haben den Eindruck gewonnen daß die Bestimmung der Potentialdauer Verteilungen (AP Dauerhistogramm) bereits mit *einem* Vielkanal-Analysator (CAT) zuverlässig gelingt und mit der klinischen Erfahrung und mit einer Fourier Analyse des EMG übereinstimmt.

METHODIK

Die Aufzeichnung der Elektromyogramme erfolgt mit handelsüblichen Dise-Nadelelektroden Durchmesser 0,4 mm, Vorverstärkung in der Tektronix Vorverstärkern Type 122 oder in einem selbstgebauten 4-kanaligen Gegentaktverstärker und die Registrierung auf einem Honeywell-M gnetbandspeicher 8100 Jeweils drei Muskeln (Stirn Oberlippe Kinn) von der erkrankten Gesichtshälfte wurden simultan mit einer Kontrolle der gesunden Oberlippe abgeleitet. Zur Analyse im Erlanger Physiologischen Institut wurden die wichtigsten Aufnahme zusammengeschnitten Hier wurden die Aktionsströme nach variabler Verstärkung

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COMPUTER ANALYSE VON FAZIALIS-ELEKTROMYOGRAMMEN I

Dauer der Aktionspotentiale

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Aus der Universitätsklinik und Poliklinik für Hals Nasen-Ohrenkranke Würzburg und dem I Physiologischen Institut der Universität Erlangen-Nürnberg Deutschland

Die auf Magnetband gespeicherten Elektromyogramme von 9 Patienten mit peripheren Fazialisparesen wurden statistisch ausgewertet, indem ein automatisches Rechenwerk (CAT) durch Klassierung der Potentialdauern sog Dauer Histogramme lieferte und durch Klassierung der elektrischen Pausen sog Intervall-Histogramme erstellte Zur Absicherung gegen Verfälschungen der Ergebnisse durch störende Überlagerungen diente die Aufzeichnung des Pegeldiagramms. Aus demselben Grund wurden die Verteilungen ausgesondert bei denen D-Histogramm und I Histogramm im gleichen Zeitbereich Maxima aufweisen Gegenüber den Werten der gesunden Fazialismuskulatur wiesen die Aktionspotentiale bei Neurapraxie und Axonotmesis jeweils charakteristische Verlängerungen der Potentialdauer auf Damit empfiehlt sich das Verfahren auch für die Kehlkopf Elektromyografie und für neurologische Fragestellungen

Für die Diagnostik peripherer Fazialisparesen liefert die klassische Elektromyographie die wichtigsten Unterlagen Lähmungstyp Schweregrad und Erholungstendenz können mit ihrer Hilfe recht sicher beurteilt werden Sie versagt bei der Fruherkennung der beginnenden Degeneration von Nervenfasern weil die typischen Denervierungszeichen erst nach der ersten Lähmungswoche sichtbar werden Hier sind neuere Untersuchungstechniken leistungsfähiger Die Messung der Latenzzeit der Nervenerregbarkeitstest und die Bestimmung des Intensitäts Zeitdiagramms (Taverner 1965 Laumans 1965 Richardson, 1963) Die beiden letztgenannten Tests wurden wiederholt empfohlen ihre Fehlerbreite ist jedoch noch hoch während die Leitgeschwindigkeit wegen der sehr variablen Verzweigung des Fazialisstammes nicht präzis zu bestimmen ist (Symposium Kopenhagen 1963 Löhell 1965) In dieser Phase einer noch nicht allgemein akzeptierten Untersuchungstechnik mußte die Frage auftauchen, ob die statistische Auswertung des Elektromyogramms (EMG) mit Hilfe von automatischen Rechnern nicht weitere Aufschlüsse liefern kann

Die Computer Analyse des EMG ist in der Literatur bisher nicht aufgetaucht als Ansätze kann man die Fourier Analyse von Interferenzmustern

Herrn Professor Dr W D Keidel zum 50 Geburtstag dankbar gewidmet.

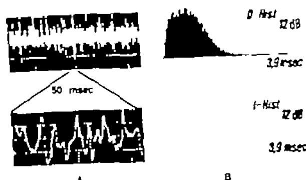


Abb. 2. I der Abl it g der gesunde Muskulat (A) ist da I terferenzmu ter on zahlreichen Aktionspotentialen ktiver motorischer Einheiten sichtbar Zwei erschiedene Zeitbasen des Kathodenstrahl erl ben die Ansicht der Registrierzeit on 1 Sek ode sowie eines Ausschnittes mit höherer Zeits flösung — Rechts (B) gibt da Potential dauer-Histogramm die Vert ilung der orkommenden Aktionspotential-Dauern nd das Intervalldauer-Histogramm die Vert ilung der P usen wieder (fü die Registrierzeit on 30 sec.

I beiden Histogrammen endet die Abszisse bei 3,9 msec Diskriminationspeg l 12 dB über dem Bezugswert.

die herkömmliche Auswertung gestattet Mit Lupe Zirkel und Maßstab wäre eine bestimmte Zahl von Potentialen auszumessen es wären arith metische Mittelwerte zu bilden und evtl umständlich die Streuungen zu berechnen. D s Rechenwerk klassiert dagegen automatisch und gibt im *Potentialdauer-Histogramm* eine Verteilung der Aktionspotentialdauern von aktiven motorischen Einheiten in grafischer Darstellung über eine statistisch ausreichende Zahl (Abb 2 rechts) Ein Blick genügt, um sich über die vorkommenden Potentialdauern deren Häufungen und Streuungen zu in formieren Dagegen sind Informationen über Potentialformen und Aktivi tätsmu ter darin nicht explicite enthalten In einer anderen, stärker auf die M thodik eingehenden Arbeit (Spreng *et al* 1967) wird u a. gezeigt, daß die Bewegungsintensität als Parameter jedoch nicht zu wesentlichen Veränderungen des Histogramm führt Ebenso wird dort belegt, daß der eben erkennbare Gipfel am linken Rand der Verteilung nicht etwa kürzesten Potentialdauern entspricht, sondern durch die Auszählung feinster Span nungsspitzen, z. B durch das Eigenrauschen des Netzwerkes und der Musku latur vorgetäuscht wird. Je niedriger der Diskriminationspegel, desto zahl reicher die miterfaßten Rausch Spitzen, und desto stärker muß dieses Arte fakt hervortret n.

Jedes Aktion potential hat eine Spitze und verbreitert sich zur Basis hin, wo die Potentialdauer zwischen Verlassen und Wiedereintreten in die elektrisch Nullin g messen wird (vgl Jasper & Ballem 1949 Buchthal, 1958) Wegen des erwähnten Eigenrauschens und infolge der Überlage rungen kann eine automatische Auszählung der absoluten Potentialdauern nicht gelingen, man muß sich mit Mes ungen nahe der Null pannung be

(Wahl des Diskriminationspegels) einem Schmitt Trigger mit kontantem Trigger pegel zugeführt. Die dadurch ausgelösten Rechteckimpulse mit einer Impulsdauer die der Pegelüberschreitung entsprach steuerten mit den aufsteigenden bzw absteigenden Flanken je einen Multivibrator deren 30 µsec Impulse als Zeitmarken für die Durchgänge am Triggerpegel (konstant vier Volt) benutzt wurden Die Markierungen der Überschreitung wurden zum Starten eines CAT Computers benutzt Die Markierungen der Unterschreitung wurden zum Zurück setzen des CAT benutzt wobei jeweils eine 1 in die eben erreichte Speicherzelle eingeschrieben wurde Nach ausreichend langer Zählung ergab sich eine Verteilung der Impulsdauern im sog Potentialdauer Histogramm mit der Häufigkeit in der Ordinate und der Impulsdauer in der Abszisse (vergleiche Abb 1 mit dem Blockschaltbild) Klassiert der CAT-Computer nur die Zeitintervalle zwischen den Überschreitungen des Triggerpegels, so entsteht das sog Intervall-Histogramm Dieses stellt eine Verteilung dar mit der Häufigkeit in der Ordinate und den Intervalldauern zwischen Muskelaktionspotentialen in der Abszisse

Nach Übernahme auf Lochstreifen wurden die Daten in den Linc 8-Computer gelesen und einer Behandlung zur übersichtlicheren Gruppierung und Aufzeichnung unterworfen Zur Abrundung der Beurteilung wurden die Elektromyogramme gleichzeitig über einen Verstärker mit großer Zeitkonstante zur Gewin nung eines sog integrativen Pegel Zeitdiagramms einem *xy* Schreiber (Mosely 2 D) zugeführt

Ausgewertet wurden die Registrierungen von 9 Patienten in Form von 390 Histogrammen Wichtigste Beobachtungszeit war eine willkürliche Dauerkon traktion (z B Mundspitzen) von 30 bis 60 Sekunden

ERGEBNISSE

Wenn der liegende Patient absichtlich entspannt, herrscht in den Ableitungen von der gesunden Gesichtsmuskulatur gewohnlich elektrische Stille Mit zunehmender Willkürinnervation (Sprechenlassen Mundspitzen Lid schluß usw mit ansteigender Intensität) verdichten sich die Aktionspotentialfolgen zu einem Interferenzmuster In der Abb 2 ist links eine Ableitung vom gesunden M orbicularis oris so aufgezeichnet daß gleichzeitig die Akti vität während einer Sekunde (im oberen Strahl langsame Zeitbasis) und ein Ausschnitt von 50 msec Dauer (im unteren Strahl schnelle Zeitbasis)

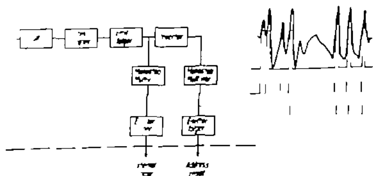


Abb. 1 Blockschema der Diskriminati n schalt g (El lh lt n Im T l)

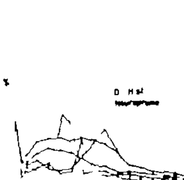


Abb. 5.



Abb. 6.

Abb. 5. Zurücktreten kurzer Aktionspotenti l und Z nahme erbreiterter Ablauf in der gelähmten Facialismusk l tur. Fünf Potentialdauer-Histogramme nach den Elektromyogrammen an fünf l icht Paresen (Neurapraxie) Etwa gl iche Diskriminationspegel bei allen Durchläufen 12–18 dB über Bezugswert.

Abb. 6 Überhandnehmen la gsamer Potentialablä f l der degenerierenden Facialism s kulatur. Fünf Potentialdauer-Histogramme nach den Elektromyogrammen aus fünf verschiedenen Muskel mit schwerer Parese (Axonotmesi) an drei Patienten. Etw gleiche Diskriminationspegel bei llen Durchlä f 12–18 dB über Bezugswert.

Abbildung 3 B zeigt dazu, wie die Verteilung der Intervallzeiten vom Diskriminationspegel abhängt.

Darüber hinaus k nn das Intervall-Histogramm als Grundlage einer quantitati en Bestimmung der Innervationsdichte an der Ableitungsstelle dienen Erstellt der Computer mehrere Intervallhistogramme sukzessiv während einer Dauerkontraktion, so läßt sich auch die Ermüdung der Muskulatur als Parameter erfassen.

Um ine Basis der Beurteilung zu schaffen, wurde jeweils eine Ableitung au der nichtgelähmt n Seite der Patienten mitregistriert. Diese gesund erscheinende Fazialismuskulatu hatte sehr einheitlich kurze Aktionspotential-D uern (Abb. 4)

Ohne große interindividuelle Unterschiede präsentierten sich auch die Analysen der paretischen Muskulatur Bei leichten Paresen mit rascher Rückbildungstendenz und hne nachweisbare D nervierungszeichen ergab ich eine relative Abnahme der kurzdauernden Aktionspotentiale und eine mäßige Zunahme von Potentialdauern auf 1,5 bis 2,5 Millisekunden (Abb.) Die Dauer Histogramme zeigten eine Andeutung von Zweigipfligkeit.

Die Verschiebung des Spektrum zu trägeren Spannungsabläufen trat rh bli h stärker hervor bei Ableitungen au der paretischen Fazialismuskul tur mit Denervierungstendenz. Sämtliche Analysen dieser Gruppe (Abb 6) boten Verteilungen mit iner Massierung der Potentialdauern zwischen 1,5 und 3 Millisekunden. Es handelt sich um unmittelbare Übertragungen der Computerwerte in das Diagramm Zur stati tischen Absicherung wurden diese Verteilung kurven mit seh unterschiedlich hohen Gipfeln einer Nor

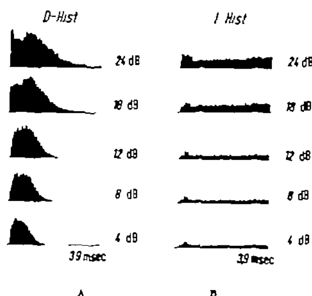


Abb 3

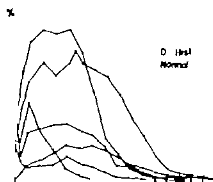


Abb 4

ABB. 3 Aktionspotentialdauer Histogramme (A) und Aktionspotential Intervall-Histogramme (B) in Abhängigk it vom Diskriminatio pegel Ausw rtu g ei er EMG-Registrierung eines gesund n Musc orbicularis oris (R G) bei kräftiger Innervation über in Zeit v n 30 sec

ABB. 4 Sechs Pot ntiald u r Hist gramm nach den Elektromyogramm n au de gesund n Gesichtsmu kulatur on sechs Patienten mit B lischer Facialisparese der Geg nseite Etwa gl iche Diskrimin tionspegel bei all n Durchläufen 12–18 dB über Bezugswert

genügen oder sich bei Wahl eines hoheren Pegels überhaupt auf eine Bewertung der Verteilung beschränken die dann über die relative Häufigkeit von erfaßten Potentialen insbes. über deren Dauern unterrichtet In Abb 3 sind links fünf Aktionspotentialdauer Histogramme wiedergegeben die fur denselben EMG-Abschnitt bei Wahl von fünf Diskriminationspegeln er stellt wurden Die geschwärzten Flächen haben — unter Abzug der artefizl ellen Kurzzeit-Gipfel — die Form von Poisson Verteilungen mit einem pegelabhängigen Gipfel zwischen 0 4 und 1,2 msec Trägt man die Gipfel punkte in ein Diagramm ein mit der Potentialdauer in der Abszisse so kann man auf die wahre Potentialdauer gemessen an der Nullinie extra polieren Dazu ist natürlich die Kenntnis der aktuellen Diskriminationsschwelle Voraussetzung Spreng hat zum Vergleich aller Histogramme einen einheitlichen Bezugswert definiert

Während die leichte Innervation eines Muskels nur wenige voneinander abgesetzte Aktionspotentiale produziert werden mit zunehmender Aktivität die elektrisch *stummen Intervalle kürzer Zuletzt überlagern* sich Potentiale und täuschen scheinbare, übergroße Potentialdauern vor Die Auswertung von Potentialdauer Histogrammen wird sinnlos wenn der Quotient Aktivitätszeit/Pausenzeit einen *bestimmten Wert überschreitet* Demnach ist die Auszählung der Intervalle das *Intervall Histogramm* eine Voraussetzung für die Auswertung von Dauer Histogrammen (vergl Spreng) Die

Diskriminationspegel erfolgen, um Störungen in der Nähe der Potentialnullage zu vermeiden. Wichtiger als eine Messung von absoluten Potentialdauern erschien uns der Vergleich zwischen gesunden und kranken Muskeln, und hier stellte sich eine charakteristische Differenz der Häufigkeitsverteilungen heraus. Die schweren Lähmungen mit Denervierungszeichen boten alle besonders hohe Anteile von langen Potentialdauern.

Man muß berücksichtigen, daß die Auskunft über Potentialdauern eine gefilterte Information ist. Ihr Nachteil ist, daß andere Parameter, z. B. die Potentialform, herausfallen. Ihr Vorteil dagegen, daß man allem Anschein nach weitgehend unabhängig wird von der noch vorhandenen Innervationsdichte und der Position der Ableitungselektrode. Man darf damit rechnen, daß die Nadelspitze zwischen 0 und 20 motorische Einheiten erfaßt. Die statistische Auswertung über die Registrierzeit von 30–60 sec formt daraus eine abgerundete Verteilungskurve wegen der biologischen Streuung und der unvermeidlichen Unruhe in der Nullinie.

Nachdem die Erprobung dieser Auswertemethode schon an einer kleinen Zahl von Kranken ein anscheinend klares Resultat erbrachte, muß es weiteren Verlauf k ntrollen an einer größeren Zahl vorbehalten bleiben zu überprüfen, welche Vorteile sich für die klinische Diagnostik und Indikation darau ergeben. Insbesondere müßten mehr Frühuntersuchungen statt finden, um evt. neue Gesichtspunkte für die Frühindikation zur Fazialisde k mpression (Miehlke 1960, Wigand, 1967) zu gewinnen. Die Übertragung der Auswertung auf Kehlkopf-Elektromyogramme wird vorbereitet. Auch für neurologische Fragestellungen kommt diese Technik in Betracht. W ert oll erscheint die Methode schon jetzt deswegen, weil bei langdauernden peripheren Paresen andere Maßnahmen, z. B. auch der Nervenerregbarkeitstest, manchmal versagen, andererseits Fibrillieren nicht immer sichtbar wird und besonders in der Fazialismuskulatur schwer zu erkennen ist. Wenn das Potentialdauer-Hi togramm — unter Berücksichtigung des dazugehörigen Intervall-Hi togramms — auch in diesen Fällen eine sichere Beurteilung zuläßt, und dafür sprechen die vorläufigen Erfahrungen, dann würde dies den technischen M hraufwand ausgleichen.

SUMMARY

The tape-recorded electromyograms of ni p tients with peripheral facial paral y were fed into CAT computer. The duration of both muscle action potenti l nd the interval between them were counted. The results of th analysis are gi en as tim duration histograms nd time int rval histograms. The tim of ana l sis, sually 30–60 seconds, w checked by integr ting lev l recorder which rejected period f disturbi g ise. In contrast t the ormal musculature all samples from the paretic musculature showed an increased duration of action potentials. Cases with onotmesis seemed to be distinctly different from those with neurapraxia.

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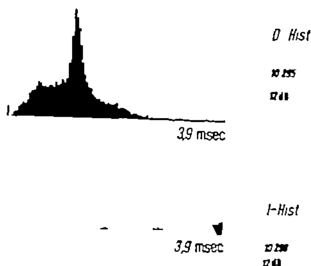


Abb. 7 Zweigipflige Kurve im Aktionspotentialdauer Histogramm einer Patientin im Stadium der Regeneration nach Bellscher Lähmung mit Axonotmesis vor 18 Monaten Das Intervall Histogramm belegt, daß die Pausen durchweg länger sind als die Potentialdauern

mierung unterzogen an dem Befund einer einheitlichen starken Rechtsverschiebung also zu längeren Dauern änderte sich dadurch nichts

Die letzte Abbildung (Abb 7) zeigt das Dauer und Intervallhistogramm einer Patientin mit weitgehend wiederhergestellter Motorik etwa 18 Monate nach peripherer Fazialisparese mit Degeneration (Axonotmesis) Hier fällt auf daß ein erster Gipfel mit Potentialdauern um 0 6 msec wieder vorhanden ist während ein zweiter steiler Gipfel mit Werten um 1 3 msec der Verteilungskurve aufgesetzt ist, offensichtlich ein Äquivalent von Lähmungsresten Das Intervallhistogramm zeigt dazu parallel die noch rel dünne Innervation und beweist zugleich daß in den interessanten Zeitbereichen (0,5 bis 2 msec) keine die Analyse störenden Überlagerungen vorhanden waren

DISKUSSION

Die auf Magnetband gespeicherten Elektromyogramme von 9 Patienten mit peripheren Fazialisparesen wurden der Behandlung im automatischen Rechner unterzogen eine erste Analyse sortierte Potentialdauern und Intervalle Dadurch wurde die Auszählung von Potentialdauern über eine statistisch ausreichende Zahl ermöglicht Maßgebend für die Wahl dieses Parameters war unser Eindruck gewesen daß bei EMG Ableitungen aus gelähmten Muskelabschnitten noch häufiger als von Buchthal beobachtet verlängerte Aktionspotentiale sichtbar werden Die in unseren Potentialdauer Histogrammen anzutreffenden normalen und pathologischen Werte liegen zwar generell niedriger als die in Buchthals Tabelle jedoch bezogen sich seine manuellen Messungen auf die Gesamtdauer mit allen Phasen des Potentials Unser Computer tastete dagegen nur Spannungsstöße in einer Richtung ab Außerdem mußten unsere Zählungen auf einem bestimmten

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AUDIOMETRIC FINDINGS IN BRAIN STEM LESIONS

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The findings obtained from a person l case-mat rial of 24 subjects llowed for definition of a clinical audiometric pattern of brain-stem lesions. The analysi of these data showed th following facts (1) In BS pathology the tone thresh ld is frequently altered (different aspects f neural-type loss without recruitment) (2) I some cases with little or o alteration of the ton threshold a poor discrimination of normal speech is present (tone-speech dissociation) (3) Poor articulation curves for low-redundancy (r sensitized) speech tests re frequently found nd there xist some quantitative nd qualitative discordan ies between the different tests even discriml atio f swi ging speech is often altered. (4) I many cases, the hearing defect is bilateral, although it is lway prevalent on one side only thus showing its derivation from a lesion f th hearing paths. (5) Th affected ear (or the prevalently impaired ear) has been found t be h mo- or contralat ral to the site where th lesion of th b s. prevails in an equal number f cases. (6) Although ll the lements of a complete audiometric in estigation lead to a general diagnosis f lesion f the central hearing paths in the b.s., the precise localization can be established with th id f other neurological signs.

Audiometric investigations of lesions of the central auditory paths have now become very fashionable and the question is being debated by an increasing number of investigators.

In the course of about a decade experience allowed the establishment of a series of tests (an extensive review of the literature on this problem can be found in a paper by Bocca & Calearo (1963)) which, from a clinical point of iew have been found to be practical and adequate for this par ticular branch of audiometry

Sen itized vocal tests devised by Bocca *et al* (1955) have all owed—for in tance—the definition of an audiometric pattern of cortical dysacusis" which offers di gnostic evidence of lesions of the temporal-parietal cortex.

Conversely the continuous variability of data obtained has not yet al lowed a clear-cut definition of the audiometric alterations of lesions f the auditory tract at the brain-stem level

W know that in this part of the CNS a large number of extremely complicated nervous circuits are found in a limited space neuro-anatomy and neurophysiology consider these as a part of the hearing system, althou h their functional significance is yet nearly unknown

Therefore a lesion of the same exten ion may affect, at this level a m ich larger portion of the auditory tract than in the cortex.

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Eingega g n am 1 J nu r 1968

An examination of these data indicates that auditory integration most probably requires the collaboration of all the nervous circuits which—on a purely morphological basis—we are accustomed to define as levels of the auditory tract

Thus, we might not be justified in trying to split up the auditory system even from a functional point of view with the aim of establishing different and increasingly complex stages of integration

However experimental neurophysiology has shown that integrational processes of any sensorial message start right from the periphery of the specific nervous path and that they become more complex as they proceed to the cortical area. Evidence for this statement can be found in brain stem lesions. Grahe reports one case of crossed speech deafness in a lesion of the lateral lemniscus with preservation of tonal hearing, and similar findings have been reported by Brunner (1936) Güttich (1940) de Crinis (1942) Falkenberg (1941) and—more recently—Kos (1955) Parker *et al* (1962) Antonelli *et al.* (1963) Antonelli & de Mitri (1963) and Elekel *et al* (1966)

This phenomenon, which we have labelled "tone-speech dissociation may even be strictly monolateral and cannot therefore derive from a gnosic" perceptive alteration. It may be assumed that the tone-speech dissociation is due to disgregation of some particular subcortical level of elaboration and integration of the auditory message

Due to this fact, the adoption of vocal tests, aiming at a global functional exploration of mechanisms of auditory integration, appears to fulfill the clinical and diagnostic purpose of this type of research.

Alteration of these mechanisms may reach different degrees, as shown by the f ct that, along with severe tono-vocal dissociation, cases of brain stem lesion are found where the hearing defect for speech becomes evident only by using vocal material whose discrimination is more difficult "sensitiza tion of this m terial has been obtained by different methods such as frequency distortion (Bocca *et al* 1955 Jerger 1960 Elekel *et al.*, 1966) the use of lists of monosyllables that are difficult to recognize (Goldstein *et al* 1950) the use of lists of w rds delivered at a high level of intensity or in presence of noise (Greiner & Lafon, 1957) time-compression (Calearo & Lazzaroni, 1957) periodic interruption (Bocca *et al* 1957) by vocal message periodically oscillating between one ear and the other—swinging peech (Hennebert, 1955 Bocca *et al* 19 7 Calearo, 1960 Antonelli *et al.*, 1963) and Mat ker test (1958) based on resynthesis of the two semi-spectres of the message delivered simultaneously one to each ear (Hayashi *et al* 1966)

Th adoption f these tests ha yielded promising results which are often comparable between themselves. These results will be discussed—along with th ones deriving from our case material—in a attempt to defin brain-stem dysacu is.

Furthermore, the occasional injury to adjoining nervous structures with different function may originate a series of varying audiometric patterns.

However the identification of such variations becomes sometimes very difficult on account of the impossibility of establishing the microscopical limits of the lesion and—on the other hand—of our ignorance as to the exact functional significance of the nervous relays affected.

Thus, the problem of dysacusis in brain stem lesions should be tackled from a merely clinical point of view and we have endeavoured to define the differential aspects of its audiometric pattern giving however due consideration to the point that—as happened before in this field and in others—clinical findings may suggest interesting clues for further experimental investigations. Starting with the pioneer work of Grahe (1896) a considerable incidence of auditory troubles has been pointed out in brain stem diseases. These aspects along with problems connected with the relationship between the ear affected and the level and side of brain stem involved have been dealt with in a number of papers which have been extensively reviewed by Calearo (1958).

It should be stated that the hearing defect usually consists in a more or less severe hearing loss for pure tones accompanied by a proportional alteration of SRT and DS.

Later on in the course of these investigations, a large number of tests have been devised and elaborated with the aim of focusing the qualitative aspects of hearing troubles.

Among these tests investigations with pure tone material aim at analyzing the particular aspects of auditory integration which are characteristic of every level of the brain stem.

Further it has been tried to establish a relationship between level and function although the impossibility of microscopical analysis of the lesion and the poor knowledge of neurophysiology gave rise to considerable difficulties.

Therefore discrepant and sometimes conflicting data have been obtained, some of which are often debatable such as the finding of an abnormal tonal adaptation on affected frequencies (Parker *et al.* 1962, Pestalozza & Cioce 1962, Sörenson 1962, Eickel *et al.*, 1966) the results of lateralization and localization tests (Jongkees & Veer 1957, Sanchez Longo *et al.* 1957, Walsh 1957, Sanchez Longo & Forster 1958, Matzker & Welker 1959, Sala & Poloni 1962, Nordlund 1964, Schindler & Demichelis, 1966) as well as tests based on binaural beats (Demichelis *et al.*, 1966).

Other tone tests yielded positive (although inconstant) results and show—even in normal subjects—a considerable variability of findings: these are the tests of the influence of contralateral masking with white noise on hearing adaptation (Brunetti 1960, Maspétiol *et al.*, 1961), tests based on binaural supplementation or inhibition (Chocholle 1960, Maspétiol *et al.* 1960) and studies on the reaction time or identification time of a supraliminar tone stimulus (Chocholle 1954, Maspétiol *et al.* 1960).

An examination of these data indicates that auditory integration most probably requires the collaboration of all the nervous circuits which—on a purely morphological basis—we are accustomed to define as levels of the auditory tract

Thus, we might not be justified in trying to split up the auditory system even from a functional point of view with the aim of establishing different and increasingly complex stages of integration

H wever experimental neurophysiology has shown that integrational processes of any sensorial message start right from the periphery of the specific nervous path and that they become more complex as they proceed to the cortical area Evidence for this statement can be found in brain stem lesions. Grahe reports one case of crossed speech deafness in a lesion of the lateral lemniscus with preservation of tonal hearing, and similar findings have been reported by Brunner (1938) Güttich (1940) de Crinis (1942) Falkenberg (1941) and—more recently—Kos (1955) Parker *et al* (1962) Antonelli *et al* (1963) Antonelli & de Mitri (1963) and Eickel *et al* (1968)

This phenomenon, which we have labelled "tone-speech dissociation may even be trictly monolateral and cannot therefore derive from a gnosic" perceptive alteration. It may be assumed that the tone-speech dissociation is due to disgregation of some particular subcortical level of elaboration and integration of the auditory message

Due to this fact, the adoption of vocal tests, aiming at a *global func tional* exploration of mechanisms of auditory integration appears to fulfil th clinical and diagnostic purpose of this type of research

Alteration of these mechanisms may reach different degrees, as shown by the fact that, along with severe tono-vocal dissociation cases of brain stem lesion are f und where the hearing defect for speech becomes evident only by u ing vocal material whose discrimination is more difficult "sensitiza-tion of this material has been obtained by different methods such as fre quency distortion (Bocca *et al* 1955 *Jerger* 1960 *Eickel et al* 1966) the use of lists of monosyllables that are difficult to recognize (Goldstein *et al* 1950) the use of li ts of words delivered at a high level of intensity or in presence f noise (Creiner & Lafon, 195) time-compression (Calearo & Lazzaroni, 1957) periodic interruption (Bocca *et al* 1957) by vocal messages periodically oscillating between one ear and the other—swinging peech (Hennebert, 1955 Bocca *et al* 1957 Calearo, 1960 Antonelli *et al.*, 1963) and M tzker test (1958) based on resynthesis of the two semi-spectres of the message deli ered simultaneou ly one t each ear (Hayashi *et l* 1966)

Th doption of these tests has yielded promi ing result which are often comparable between themselves. These result will be discu sed—along with the ones d ri ing from our case material—in a attempt to define brain stem dy acu is.

TABLE 1

BP Bulbo-pontine lesion; PM ponto-mesencephalic lesion M, mesencephalic lesion Diff diffuse lesion + means altered discrimination or neurological signs on that side (L, left, or R, right)

No	Type of lesion	Portion of b.s. involved L	Portion of b.s. involved R	Audiometric findings: Pure tone threshold L	Pure tone threshold R	Discr for normal speech L	Discr for normal speech R	Discr for swinging speech	Discr for distorted speech L	Discr for distorted speech R	Discr for time-compressed speech L	Discr for time-compressed speech R
1	Polioencephalitis	M +	M +	–	–	–	–	–	–	–		
2	Central vestibular syndrome	BP +	BP +	–	–	–	–	–	–	+	–	
3	Ponto-peduncular syndrome	PM +	–	+	+	–	–	+	+	–	+	
4	Pseudotumoral encephalitis	Diff.		+	+	–	–	+	+	+ +	+	+ +
5	Right retro-olivary syndrome	B +	B +	–	–	–	–	–	–	–	–	
6	Inflammatory process of the b.s.	BP +	–	–	–	–	–	–	+	–	+	
7	Neurolues	Diff		–	–	–	–	–	+	–	+	
8	Neoplasm of b.s.	BP + +	BP +	+	+	–	+	+	–	+	–	+
9	Neoplasm of b.s.	PM + +	PM +	–	–	–	+	+	–	+	–	+
10	Neoplasm of b.s.	M +	M + +	–	–	+	–	+	+ +	+	+	+
11	Neoplasm of b.s.	BP +	BP +	–	–	–	–	+	–	–	+	+
12	Neoplasm of b.s.	M +	M +	+	+	–	–	–	+	+	–	–
13	Neoplasm of b.s.	BP +	BP +	+	+ +	–	–				–	–
14	Cerebellar tuberculoma	–	BP +	–	+	–	–	+	–	–	–	–
15	Diffuse vasculopathy	BP +	BP +	–	–	–	–	–	–	+	–	
16	Metastatic neoplasm of b.s.	BP +	BP +	+	+ +	+	–		+	–	+	–
17	Syringobulbia	BP +	BP +	+	+	–	–	+	+	+	–	–
18	Multiple scler	Diff		+	+	–	–	+	–	–	–	–
19	Multiple scler	Diff		–	–	+	–	–	–	–	–	–
20	Multiple scler	Diff.		–	–	–	–		–	–	–	+
21	Multiple scler	Diff		–	–	–	–		–	–		–
22	Multiple scler	Diff		–	–	–	–	–	–	–	+	–
23	Nucleo-reticular vestibular syndrome	BP +	BP +	–	–	–	–	–	–	–	+	
24	Nucleo-reticular vestibular syndrome	BP +	BP +	–	–	–	–	–	–	–	+	

CASE MATERIAL

Twenty four subjects admitted to the Neurological Clinic for lesions of the BS have been studied

This case material comprised tumours (8 patients) multiple sclerosi (5 patients) inflammatory conditions of unknown etiology (5 patients) vascular lesions (5 cases) and diffuse neurosyphylis (1 patient)

In 17 cases, it has been possible to establish with good approximation

the longitudinal level where the lesions were more extensive (bulbar in one case bulbo-pontine in 11 ponto-mesencephalic in 2, and mesencephalic in the remaining 3 cases)

On the basis of neurological data, it has been established that the lesion was strictly monolateral only in 3 patients, whereas in 10 patients there existed signs of damage prevailing on one side of the BS

Table 1 shows the data concerning all the cases examined in the present research a detailed description of each clinical pattern can be found in partial case reports already published elsewhere (Antonelli *et al* 1963 Antonelli & de Mitri, 1963 Mosciaro & Pignataro, 1964)

METHODS

All patients have undergone the common laboratory tests, neurological examination and—if necessary—vestibular tests.

The audiometric examination of the 24 patients started by determination of t nal threshold by air and bone conduction followed by adaptation and recruitment tests, whenever needed.

Afterwards, discrimination of normal and sensitized speech material (time-compressed speech, distorted speech, swinging speech) has been ex amined.

Normal material consisted of tape-recorded lists of 10 meaningful 5-word sentences.

Accelerated material consisted of sentences of the same type subjected t a particular system of time-compression. This system is based on the use of 2 coupled tape-recorders furnished with a device for variation of the recording time which does not alter the frequency of registered sound This device makes use of a mechanic apparatus moving the magnetic head along with the tape in order to keep the relative speed unmodified To obtain this result the tape is not played back by a fixed head, but instead by a group of moving heads, as shown by Fig. 1 Through this system, it becomes possible to obtain a variation of the speed of words from a value of 150 words/minute (being the normal value for Italian speech) to 350 words/minute without any modification of the acustic spectrum (Lietti 1958)

Distorted material consi ted of sentences of the same type as the preceding ones, ha ing undergone a particular procedure of filtration and distortion Filtration was obtained by progressive attenuation of frequency bands 400–800 1600–3200, 3200–6400 The all-over effect can be compared t the one f a low pass filter at 500 c/s.

Di tortion has been obtained by passing the filtered material through a ring modulator built according to the classical scheme capabl of produc ing all the combination tones of incoming sound-structures

The winging-speech test has been performed by oscillating periodically the n rmal peech m terial between one ear and the other for qual period

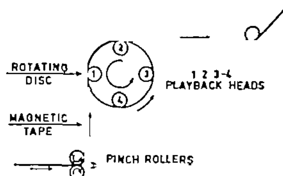


FIG. 1 See text.

of time, so that each ear receives half of the message The period of oscillation varies between one and 40 alternations/sec, thanks to the use of a Grason–Stadler electronic switch

Average discrimination values obtained by all these sensitized speech tests have been studied on normal subjects, bearing in mind their I Q (Teatini, 1961 Calearo & Hahn 1964)

The maximum discrimination at a comfortable hearing level reaches 80% for time-compressed and distorted voice Discrimination for swinging speech always reaches 100% regardless of the period of alternation The reasons for using speech material instead of tones for audiometric tests have already been stated (Bocca & Calearo 1963) we should only like to stress here that speech is a more adequate material as it allows for exploration of central levels of auditory integration and for a global test and can be performed regardless of tone deficits which are so frequent in b s. lesions.

Obviously the integration of verbal material requires the intervention of nervous mechanisms not being strictly auditory and therefore every method basing on this material has some particular requirements. The first one is to use short meaningful sentences instead of words In this way errors due to deformation of significance caused by the sensitization processes can be reduced to a minimum

Further it is indispensable to check the average discrimination valu for sensitized verbal material in normal subjects and to correlate it with the I Q

Such a control has shown that the discrimination value rises until it reaches a maximum corresponding to an I Q level of 107 (this being the average I Q level of the Italian population) From this point onwards the discrimination score remains unchanged even with a rising I Q One may therefore conclude that the individual variation of extra auditory mental factors cannot lead—in average individuals—to any substantial difference of discrimination for sensitized verbal material

RESULTS

Audiometric Findings

(a) Pure tone audiograms

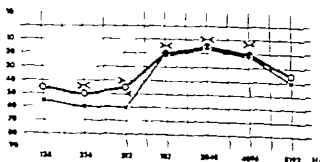
In 15 out of 24 cases examined the hearing threshold for pure tones was normal or showed only transmission-type alterations. In other 6 cases, a monolateral or—more frequently—bilateral deficit on acute tones has been found. The last 3 cases showed particular findings in case No 13 the threshold was increased at 1000 cps (50 dB) reaching its maximum at 4000 dB (70 dB) with a slight improvement on 8000 cps In the left ear the curve was parallel but the deficit slighter In case No. 16 a neural type bilateral hearing loss for all tones up to 2000 cps was found, followed by further impairment on high tones (Fig. 2) In case No 18 an air and bone deficit limited to lower frequencies was present on both sides (50 dB) Recruitment tests have always been negative.

(b) Normal speech test

In 19 cases out of 24 the articulation score for normal sentences was in accordance with pure tone threshold Conversely in 5 cases, a tone-speech dissociation was present in one ear (in 4 cases a displacement and abnormal slope of intelligibility scores as compared to normal has been found (Fig. 3) and the fifth case showed complete mon lateral verbal deafness (Fig. 4)

(c) Swinging speech test

It has been performed in 22 subjects where a bilaterally equivalent hearing condition had been found or else where this condition could be obtained by compensation of the inten ity in the worse ear The case with monolateral speech deafness has been excluded (Fig. 4) Normal scores have been obtained in 13 out of 22 subjects. A variable deficit, reaching its maximum between 3 and 8 alternations/sec has been found in the other 9 patients.



F 2. Pure-tone audiogram of the subject No 16 (see text).

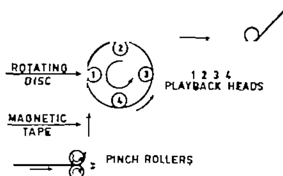


FIG. 1 See text

of time, so that each ear receives half of the message The period of oscilla tion varies between one and 40 alternations/sec, thanks to the use of a Grason–Stadler electronic switch

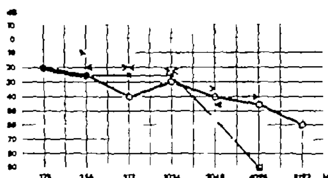
Average discrimination values obtained by all these sensitized speech tests have been studied on normal subjects, bearing in mind their I Q (Teatini 1961 Calearo & Hahn 1964)

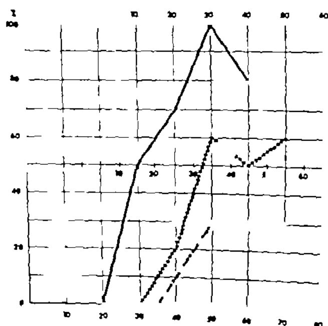
The maximum discrimination at a comfortable hearing level reaches 80% for time-compressed and distorted voice Discrimination for swinging speech always reaches 100% regardless of the period of alternation The reasons for using speech material instead of tones for audiometric tests have already been stated (Bocca & Calearo 1963) we should only like to stress here that speech is a more adequate material as it allows for exploration of central levels of auditory integration and for a global test and can be performed regardless of tone deficits, which are so frequent in b s lesions.

Obviously the integration of verbal material requires the intervention of nervous mechanisms not being strictly auditory and therefore every method basing on this material has some particular requirements The first one is to use short meaningful sentences instead of words In this way errors due to deformation of significance caused by the sensitization processes can be reduced to a minimum

Further it is indispensable to check the average discrimination value for sensitized verbal material in normal subjects and to correlate it with the I Q

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Fi 4 Tone-speech dissociation. Slight threshold impairment in the speech range frequencies of the left ear. No discrimination for the speech material in the same side. Same symbols as in Fig. 3.

Rel tionships between the Audiometric Pattern and the Site of the Lesion

In the only case with a strictly bulbar localization, the audiometric pattern h s been found to be normal. *Out of the 11 patients with a bulbo-*ponti localization, an *impairment of the tonal threshold was found in 5* f normal peech test in 2, *of swinging speech test in 4, of distorted speech* test in 6 and of *time-compressed speech test in* . *It may thus be stated* that out f 11 cases *of bulbo-pontine lesions* showed *alterations of 2 or* more tests.

All th sensitized speech tests were *impaired in the 2 cases of pontine*

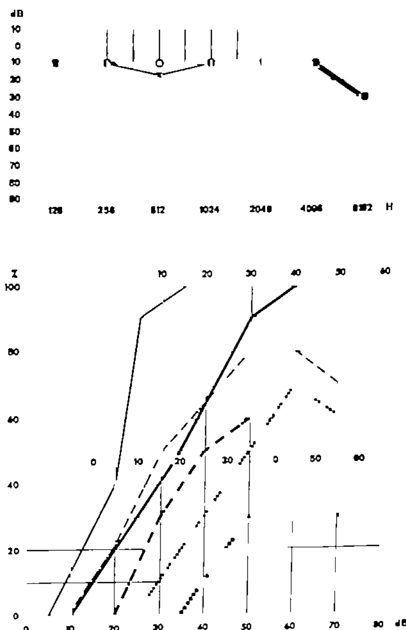


Fig 3 Tone- peech dissociation Normal p re-ton thresh ld fo the peech range frequencies. Abnormal l pe f the articulati n curves f the sensitized and non-sensitized speech material. Normal speech test. —— right ear —— left ear d torted peech-test. — — RE. — — LE. tim -compressed peech test RE, LE.

(*d*) *Distorted speech test*

Out of 23 cases tested 11 gave results in accordance with pure tone and normal speech findings Out of the other 12 8 showed a more or less marked monolateral deficit (Fig 3) and 4 a bilateral deficit Two of the latter however showed signs of unilateral prevalence

(*e*) *Time-compressed speech test*

This test also has been performed in 23 patients only In 9 cases, a unilateral and in 5 a bilateral deficit has been found

DISCUSSION

In brain-stem lesions, audiometric investigation completed by sensitized speech tests can show the presence of hearing impairment in a high percentage of cases (19 cases out of 24). This is in accordance with the statements of other investigators (Jerger 1960, 1964, Eickel *et al.* 1966).

In the remaining cases, the absence of hearing defects may offer some clues as to the limits and extension of the lesions (Group 4 described by Jerger 1964).

A comparison between brain-stem dysacusis and cortical dysacusis shows that the hearing impairment is slighter and strictly monolateral in cortical lesion, whereas it is more marked and often bilateral in brain stem lesions.

Two considerations may help explaining this difference. The first one concerns the anatomy of the region where the lesions are found. In the brain stem the hearing paths on both sides are concentrated in a limited space, whereas in the cortex, they spread out and become completely separated in the two hemispheres. Therefore equally extended lesions yield a much higher incidence of severe and bilateral impairment when they are located in the brain stem than when they are located in the cortex.

Secondly, and particularly so when tumoral lesions of the brain-stem are involved, the circulation of liquor may be hindered leading to an internal hydrocephalon, which is largely responsible for an intellectual hnul llati n of the patient.

In these cases, the defect is bilateral and present with all the different sensitized speech tests. It may recover when a normal liquor circulation is reestablished by surgery.

In 6 of our patients there were clinical signs of intracranial hypertension and 4 of these showed an important bilateral loss of discrimination for distorted speech and time-compressed speech. It should be stressed that, even under such conditions, there was a unilateral prevalence of the defect indicative of the site of the lesion affecting the hearing paths.

Another substantial difference between cortical and brain-stem dysacusis concerns the correspondence between the ear affected and the side of the neurological lesion.

In lesions of the cerebral cortex, the hearing impairment is always found on the opposite side of the affected hemisphere. On the contrary, in lesions of the BS, even in the presence of data indicating a unilateral lesion, the hearing defect may be homo- or contralateral.

When tone-speech dissociation occurs it is often contralateral, whereas, when alteration of tonal threshold are found the ear affected is always homolateral. Most likely these facts depend upon the level of the lesion, i.e. the condition changes whether the hearing paths are affected before or after crossing.

Our data suggest that tone-speech dissociation cannot be attributed to the impairment of any defined anatomical structure of the BS; nevertheless,

mesencephalic localization and *one case showed even tone hearing loss*

Out of the 3 cases of mesencephalic lesion one showed an alteration of all the tests and one an impairment of discrimination for distorted speech on both sides Positive data have been found in 6 out of the 7 cases of diffuse suffering of the BS

As far as the existence of a relationship between the level of the lesion and the impairment of the single tests is concerned the pattern of the tone-deficit showed no particular characteristics, with the exception of permanent absence of recruitment

An analysis of the relationship between tone-tests findings and the level of the lesion of the b s—whenever it could be established—shows that the *tonal threshold is altered in less than half the cases of bulbar or bulbo*-pontine localizations once in one of 3 cases of mesencephalic lesions and in half the cases of ponto-mesencephalic lesions In the only case of bulbo-pontine lesion where a strictly unilateral localization had been established the tone deficit was homolateral

The 5 cases of tone-speech dissociation included 2 bulbo-pontine and one pontine-mesencephalic lesions as well as a diffuse lesion due to multiple sclerosis

In 3 *of these cases, a relationship could be established between* the lesion of the brain stem and the affected ear the deficit for normal speech was always contralateral

Poor discrimination *for swinging speech has been found in 4 bulbo*-pontine lesions 2 ponto-mesencephalic lesions one mesencephalic lesion and 2 diffuse lesions of the BS

Out of the 12 cases showing a poor discrimination for distorted speech 6 had bulbo-pontine lesions 2 ponto-mesencephalic, and one diffuse lesions In 6 cases there were neurological signs of a lesion affecting prevalently one half of the brain stem and poor discrimination for distorted speech has been found 3 times on the same side and 3 times on the opposite side without any relationship to the height of the lesion

Poor discrimination with time-compressed speech was in agreement with the data for distorted speech both with regard to height and side of the lesion in 9 cases (4 bulbo-pontine 2 pontine-mesencephalic and 3 diffuse lesions) No agreement between the 2 tests was found in 7 cases In 3 of them, time-compressed speech test was normal whereas distorted speech test *was altered on one or both sides in one case* discrimination for distorted speech was poor on one side and for time-compressed speech on both sides in the last 3 patients discrimination for distorted speech was normal and altered only *for time-compressed speech*

No relationship between the level of the lesion and the difference between both tests could be found in 5 cases (3 bulbo-pontine and 2 mesencephalic) In 2 cases, poor *bilateral discrimination for time-compressed speech* was the only sign of hearing impairment in both cases the bulbo-pontine nuclei and the surrounding reticular formation were involved

spricht, dass lie Elem nte der audiometrischen Untersuchung die Diagnose einer Läsion der zentralen Gehörbahnen im Gebiet des Gehirnstamms ermöglichen so kann man eine genaue Di gnose der Höhenlage nur vermuten, was jedoch für den neurologischen Symptomkreis on besonderem Wert erscheint.

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it remains a typical—although not frequent—finding of brain stem dysacusis. Its degree varies from a simple displacement of SRT to intensity levels higher than those suggested by the tone threshold up to a true monolateral speech deafness.

Another characteristic of BS lesions, which has already been described, is the fact that they cause dysacusic hypoacusis, i.e. that tone deficits, which are practically absent in cases of cortex pathology, can be frequently found in BS pathology. These defects are seldom very marked and most probably derive from a functional alteration of the bulbar cochlear nuclei and/or of the auditory nerve. Further evidence for this assumption is offered by the constant lack of recruitment and by the frequent presence of abnormal adaptation values (Parker *et al.*, 1962; Pestalozza & Cioce 1962; Sörensen 1962; Eickel *et al.* 1966).

Among sensitized speech tests, an impairment of swinging speech discrimination has been found in a considerable number of cases in BS pathology. This finding remains characteristic of dysacusis due to BS lesion (Calearo 1960).

Finally, monaural sensitized speech tests with distorted and time-compressed speech have been found to agree in a majority of cases but not in all.

In the two cases with nucleo-reticular syndrome, for instance, there was a bilateral and symmetric discrimination deficit for time-compressed speech only. This defect might be attributed to a lesion of the brain stem reticular formation. Evidence for this view has been obtained by clinical observation (Mosciaro & Lignataro, 1964) and by experimental results (Antonelli 196*, 1963).

ZUSAMMENFASSUNG

Auf Grund einer persönlichen Kasuistik von ?0 Fällen beschreiben die Verfasser das klinische Bild des Gehördefektes bei Gehirnstammläsionen (GH). Man gelangt zu folgenden Schlüssen: 1) Bei der Pathologie des GH ist die Tonschwelle oft verändert und weist neurosensorielle Verluste verschiedener Art, jedoch ohne Recruitment auf. 2) Bei einigen Fällen beobachtet man neben einer unveränderten nur leicht alterierten Tonschwelle eine Herabsetzung der Verständlichkeit der normalen Stimme (Ton-Sprache-Dissoziation). 3) Häufig findet man Verständlichkeitsdefekte bei „low redundancy" (oder sensibilisierten) Sprachtests mit einigen quantitativen und qualitativen Verschiedenheiten zwischen den verschiedenen Versuchen; auch die Integration der alterierten Sprache ist oft verändert. 4) Bei [illegible]lichen Fällen ist der audiometrische Verlust bilateral, doch fast immer bedeutender auf einer Seite; dadurch kann man mit Sicherheit als Ursache eine Läsion der auditorischen Bahnen festlegen. 5) Das mitgenommene Ohr oder das Ohr, das mehr mitgenommen ist, kann sowohl auf der gleichen als auf der entgegengesetzten Seite der neurologischen Läsion liegen, die mehr oder weniger eine der Seiten des Gehirnstamms angegriffen hat. 6) Wenn es der Wahrheit ent

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CONGENITAL ABSENCE OF THE OVAL WINDOW

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A survey of 24 cases published so far is given Congenital absence of the oval window is not a welldefined clinical entity Other malformations of the middle ear structures are generally found. Hearing improvement was obtained in only one third of the cases previously published Four new cases are presented three of which were characterized also by other malformations apart from those concerning the ear such as the Klippel Feil syndrome cleft palate and facial palsy The hearing loss was bilateral and rather severe in two of the patients In the other two cases it was unilateral but also severe In all four cases explorative tympanotomy revealed different malformations of the middle ear in addition o the absence of the oval window Hearing improvement was obtained in two patients, transient in one case permanent in the other Some embryological audiological and kopho-surgical problems are discussed

Advances in reconstructive middle ear surgery during recent years have extended our knowledge of congenital middle ear malformations. Reports on congenital absence of the oval window are scarce Only 24 cases seem to have been reported so far A complete survey is given in Table 1 From this survey it appears that this anomaly does not constitute a well-defined clinical entity A variety of different malformations may also be present in different places of the organ of hearing On the other hand, the aural surgeon must not take for granted that a normal auditory meatus indicates normal middle ear structures In nearly two thirds of the cases published so far the auditory meatus was normal

Furthermore it appears from an analysis of the cases previously published that concomitant anomalies are found most often in the immediate vicinity of the oval window Thus lacking or defective stapes were reported in no less than 17 of the 24 cases, i e 70% while absence or defect of the incus was found in 17% and of the malleus in 12%

The facial nerve—next to the stapes the immediate neighbour of the oval window—was found abnormal concerning appearance course or cover in 13 of the 24 cases, i e 54%

The round window was lacking in one third of the cases.

The inner ear however was abnormal in only 2 cases (Mondini-defect in one case lack of lateral semicircular duct in the other)

Congenital absence of the oval window was reported as a bilateral anomaly in 7 cases and as a unilateral anomaly in 6 cases (information lacking

Table 1 *Congenital absence of the oval window*

+ = Definit information; – no definite information.

Author	Sex	Auricle and meatus	Other malformations: Middle ear	Inner	Facial nerve	Body	Hearing loss: Unilat	Bilat	Hearing gain: Attempted	Obtained
Krampitz	?	Meatus lacking	Stapes lacking	Mondinidef. Por int. narrow	Lacking	Normal	–			
Hough	M	Normal	Stapes encircling facial n.	Normal	Displaced	Normal	–		+	
Hough	F	Normal	Unicurate stapes	Normal	–	–				
Hough	?	Normal	Stapes-tendon absent	Normal	Bony canal extremely large		–			
Ombredanne	M	Microtia trevia	Round window lacking	Lat. semicirc. duct. lacking	–	–				+
Henner	?	–	Round window lacking	–	–	–				
Henner	?		Round window lacking	–	–	–				
Henner	?		Round window lacking	–	Hypoplastic	–				
Tabor	F	Normal	Rudimentary stapes	Normal	Displaced	Normal		+		+
Beickert	M	Auricle small. Meatus normal.	Stapes lacking	Normal	Displaced	–	+			+
Pou	F	Normal	Hypoplastic stapes	Normal	Previously damaged	Normal	+			+ Facial palsy
Pou	?	Normal	Unicural stapes	Normal	Displaced	–		+		+

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Fig. 1



Fig. 2.

In 11 case) In th majority of the cases the explorative tympanotomy was m de to study the middle ear defect but in certain cases a hearing improv ing operation was also attempted Hearing gain was obtained in 8 cases, i e ne third of the cases.

It is worth noting that the operation resulted in damage in two cases, liquorrhoe occurring in one case facial palsy in another It is also worth noting that the hearing loss in both cases was unilateral Considering the great risk in these very intricate operations, they should probably be carried ut mainly in patients with bilateral hearing loss, i.e where a handicap is present

This paper deals with four new cases which present interesting details from an embryological audiological and surgical point of view

Case 1

A 12-year-old boy (V L. R 18.9 10o3) with multiple congenital malfor mations (Fig. 1)

He was the nly child of normal parents who knew of no pathological predisposition in the family Deli ery had been normal although to some xtent phyxl had been present According to the hospital's record, most of the boy s malformation were ascert ined directly at birth.

Apart f om th nomalies of the ear the malformations found at clinical nd radiol gical examination were as f llows

H had a typical Klippel Feil syndrome with fused vert brae of th cervical nd upper thoracic pine the head apperently being placed directly on th trunk without any neck (Fig. 1) While 12 costae were found on the

TABLE 1 (*cont.*)

Author	Sex	Auricle and meatus	Other malformations: Middle ear	Inner ear	Facial nerve	Body	Hearing loss: Unilat.	Bilat.	Hearing gain: Attempted	Obtained
Fernandez	F	Meati stenotic	Ossicles and round window lacking	Normal	Displaced	Normal		+		
Nakamura	M	Narrow meatus	Stapes lacking	–	Displaced	—	+			
Nakamura	M	Atresia auris	Drum ossicles and round window lacking	–	–	Normal	+			
Nakamura	M	Narrow meati	Stapes and round window lacking		Displaced			+		
Bernstein	M	Auricle malform. Meatus normal	Stapes and round window malformed	–	Normal	–	+		+	Liquorrhoe
Gundersen	M	Auricle malform.	Uncurat. stapes	–	Uncovered	–		+		
Gundersen	M	Pinna deformed	Inc. and arcade absent	–	Normal	–	+			
Gundersen	M	Normal	Ossicles normal	–	Normal	–				+
Scheer	?	Normal	Arcade absent	–	Normal	Normal				
Scheer	?	Normal	Ossicles deform.		Normal	Normal				
Scheer	?	Normal	Stapes deform.		Uncovered	Normal				
Caplinger	F	Auricle small	Stapes lacking. Round window lacking. Cholestoma	Normal	Displaced	Hypoplasia of the face				

Radiographs of the temporal bones (including tomography in three projections, using the Polytome) This investigation was rather difficult because of the reduced mobility in the cervical spine On the right side normal conditions were seen

No true articulation was found between the jaw and the temporal bone on the left side as neither the condyle nor the mandibular fossa were present

The external auditory meatus on the left side was very narrow and in the upper and posterior part of the meatus a wedge like bone was seen the basic part of which was localized upwards approximately in the place of the temperomandibular joint and the attic (Fig. 3) In the middle ear some irregular shad ws were interpreted as the ossicles. As to the inner ear the lateral semicircular duct on the left side was somewhat hypoplastic, being smaller than the right one and of different shape The vestibule cochlea and the internal auditory meatus were present and on the whole normal

The intelligence of the boy had been estimated at about normal level by the school psychologist (IQ = 120) although it was not obvious to everybody

Audiological examination showed normal hearing on the right side On the left side it was difficult to ascertain whether hearing was present or not Everything tended t show a hearing loss of the mixed type amounting to 60–80 dB with a wider air-bone gap in the bass and hearing of shouted v ice with the B rany noise box in the right ear

On cal ric vestibular test no function was demonstrable on the left side either by hot or cold water (It should however be borne in mind that the meatu wa extremely narrow)

Expl rative tympan tomy was performed on the left side using a Lempert inci i n Th first thing met with in the posterior part of the meatus wa th wedge-like bone already seen in the radiographs. Behind this bon wl ich yielded to pre sure a fis ure was seen Pressing the bone lightly forw rd it ppeared that the dura was prolapsing in this fissure In front of the tran ersely located and wedge-like bone another fissure wa seen which w traced to about the t mperomandibular j int. In front of the lower part of the wedgelike bone a partial atresia of the m tu wa found consisting partly of cartilage and partly of bone Hav ng removed a mu h pos ible of the obliteration of the meatus, the se tu l expl rative tympan t my could be carried out In the middle ear all estiges of the os icles were lacking The round window was seen in its proper location, although it was not at all round but cleft like However n o al win l w w seen. Th facial nerve w met with in a lower location th n norm l.

N hearing impro ing operati n wa considered pos ible so n thing further w d ne

Post perati e course uncomplicated.

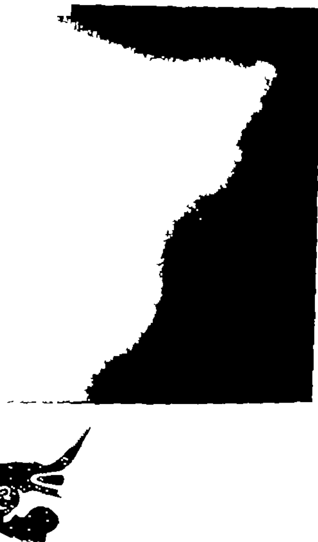


FIG. 3 Pati nt N 1 Fro t l t m graphic secti n of th l ft t mporal bon 1 Wedge-l k loos bone abo e me tus ten tle me tu 3, ochlea

right side the upper costae on the left side were lacking which produced a thoracic scoliosis curving to the right The radial bone was lacking completely in *the left forearm and the left hand set off from a thick* ulna at a right angle In addition the left thumb was lacking as well as the first metacarpal the major multangular and the navicular bones of the left hand On the tip of the nose a small dimple was present and on the left side *of the bridge of the nose recurrent infection* indicated the presence of a cyst Ophthalmological examination revealed a left sided blindness and squint without abducens paralysis or retraction of the eye-ball

Malformations of the ear *The left auricle was highly protruding hang ing down* and setting off from the head at a right angle (Fig 1) The ex ternal auditory meatus was so narrow that it was impossible to see the tympanic membrane



Fig. 4. Patient No. 2. Frontal tomographic section of the temporal bones showing the labyrinths with cochlea winding but without semicircul duct. 1 Auditory meatus 2 ossicles; 3 cochlea winding.

deaf which she attended from the 6th to the 8th year of her life after which she attended the school for the hard of hearing in Copenhagen

At the age of 13 she was admitted to our ENT ward for further examination with a special view to the possibility of making a hearing-improving operation

She was a kind and confident girl small for her age Intelligence was, according to the school psychologist somewhat below normal range.

Right external ear protruding and smaller than the left one and completely without ear-lobe

Tympanic membranes, practically speaking, normal

Right sided partial facial palsy (Fig 2)

Right-sided paralysis of the soft palate

Hearing Whispered voice could not be heard on either side and spoken voice only *ad concham* on both sides.

Audiogram showed bilateral conductive deafness amounting to 80–90 dB on both side with an amazingly wide airbone gap, threshold of bone-conduction lying on the 0 dB line Stapedius-reflexes could not be elicited on either side She was wearing hearing aid with bone-conduction receiver by means of which she managed fairly well in the school for the hard of hearing

Vestibular reflexes could not be elicited on either side on calorization either with cold or hot water

X-ray examination (including tomography) of the temporal bones showed normal pneumatization and two ossicles (malleus and incus) on both sides. The internal auditory meatus and cochlea were clearly to be seen on both sides. On the other hand, no semicircular canals were seen on either side whereas some of the vestibule was dimly seen on both sides (Fig. 4)

On operation (entering the right middle ear by the permeatal route) the following malformations were revealed The stapes was lacking completely No oval window was present In its place the bone was whitish but hard

Case 2

A 19-year-old man (J K H., 17 9 1947) operated on for cleft palate The patient had been hard of hearing since early childhood He had no otitis and no familiar predisposition was present

Normal otoscopy was found on both sides The right auricle was slightly smaller than the left one The right meatus had an abnormal direction pointing steeply upwards and forwards

Audiometry revealed a conductive lesion in both ears, rather severe on the right side The somewhat reduced bone-conduction in the treble pointed at some inner ear affection

The caloric test showed normal conditions

Radiographs including tomographic exposures of the temporal bones showed nothing abnormal

Explorative tympanotomy on the right side revealed the following characteristics While the incus was normal the stapes was severely deformed like a columella" with a rudiment of bifurcation downwards fusing directly with the labyrinth After removal no oval window was seen Due to the aforementioned acclivity of the meatus, the round window was quite inaccessible, so that it could not even be ascertained whether it was present or not

As normal labyrinthine cavities seemed to be present according to the radiographs a fenestration of the labyrinth was performed approximately at the place where the oval window should have been. The bone—being slightly more light here—was extremely thick In the fenestra a teflon piston was placed the wire-loop of which was easily closed around the long process of the incus

The course of the facial nerve could not be ascertained exactly two bony prominences were seen both of which might possibly contain the nerve one was situated in the normal place but was very thin the other —of greater resemblance with a facial nerve—was running straight through the middle ear

The operation was followed by a reduction in hearing amounting to 20 dB on all frequencies.

Case 3

A 13 year-old girl (A M K., 14 10 1952) without any familiar predisposition to deafness or deformity A smaller sister was normal in all respects and so were the parents Pregnancy and delivery normal apart from asphyxia directly after birth, which however subsided quickly Rightsided facial palsy was discovered directly after birth and deafness was ascertained early in the second year of her life When 2 years old she had her first hearing aid During early childhood she had uncomplicated measles whooping-cough chiken pox and German measles

After detailed otological examination she was sent to the school for the



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After detailed otological examination she was sent to the school for the

Case 4

An 11 year-old girl (J B P 20.8.1955) Her appearance was normal in all respects. Delivery and childhood had been uneventful No pathological predisposition in the family

The girl had never complained of any ear troubles.

The first routine hearing test at school (when she was 7 / years old) revealed a left-sided hearing loss after detailed audiological examination it proved to be of the conductive type (Fig 5)

Vestibular test normal

Radiographs of the temporal bones (including tomography in three projections, using the Polytome) showed nothing abnormal The ossicles were seen and so were both windows. The vestibule, the cochlea and the semi circular ducts showed normal conditions.

Explorative tympanotomy was carried out on the left side, using the Rosen incision By removing part of the posterior wall of the bony meatus adequate survey of th stapes and its urroundings was provided for There was a total fixation of the stapes which had furthermore no real arcade ha ing the shape of a cone (handle attached to the incus) the end of which passed like a conglomerate directly into the labyrinth, no oval window being demonstrable whatsoever The round window was of normal shape and location.

The facial nerve was passing right through the middle ear between the round window and the insertion of the malformed stapes in the labyrinth. In addition, the facial nerve was without any cover in the upper half of the middle ear section

The stapes-conglomerat was taken down after which a tiny light yellow area was observed, situ ted right behind the unco ered facial nerve and partly overhung by a bracket like projection of bone which was taken away first The yellowish area was cauti usly drilled still more thin until it appeared with a bluish pellucidity after which it was gently perforated with a fine hook Perilymph leaked out and piece by piece the pellucid shell of bone was removed until a "window had been made sufficiently wide to take teflon-piston the hook of which was closed around the long process of the incus.

Postoperati e course uncomplicated There was some vertigo and nystag mu t the left for a few days

There w a great hearing improvement which so far—one year after the oper tion—remain unchanged (Fig. 6)

DISCUSSION

The four cases here dealt with present some very interesting problems from an embryological, audiological and surgical point of view

Embryology According t Ba t & Anson (1949) the primordial footplate of the tapes is laid out not only from part of the second visceral bar

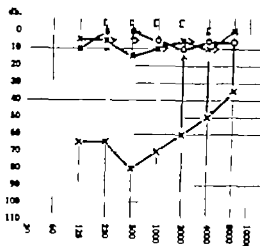


Fig 5

and impenetrable. No round window was present in its place the bone was flat, thin and pliable—membranous, so to speak Between these two areas (where the windows should have been) a ridge was passing through the middle ear possibly containing the facial nerve (which however was not explored) The incus was slightly deformed, the lenticular process lacking completely and the long process coarse and conical

In order to obtain transmission of sound the author proceeded in the following way

Using the polytomography as a guide, a fenestration was made to the vestibule the starting point being the aforementioned whitish area which was supposed to represent an undeveloped oval window On drilling it proved that this whitish bone was extremely thick A canal was drilled until perilymph leaked out A teflon piston was used to connect the incus with the vestibule the piston being as well fitted in the canal as in a cylinder and the wire being hooked on the incus, which was, however rather difficult due to the conical shape of the long process of the incus

Post-operative course uncomplicated

A remarkable hearing improvement followed TAA rising 48 dB, the child being now able to manage without hearing aid at home and with a new transistor aid air conduction with ear piece at school

Hearing gain unchanged during the first four months of control After this hearing deteriorated in a couple of months to the preoperative level

As slipping of the wire loop from the deformed incus was suspected reoperation was performed

The reoperation revealed that the fenestration was partly obliterated by regenerated bone which prevented the teflon piston from vibrating

The fenestrated canal leading to the vestibule was widened by mean of a diamond drill and a new teflon piston was placed in the canal

Hearing improved about 30 dB in the middle range but the improvement did not last for more than 2 months after which it returned to preoperative level

bone was thin the opening was more like a fenestration Consequently the hearing gain has lasted ever since the operation one year ago.

Concerning severe malformations of the middle ear—as here dealt with —a preoperative estimate of achievable hearing gain, if any is far more difficult than in other conductive lesions as, for instance otosclerosis. Neither audiological nor radiological examinations will render sufficiently certain hints concerning the possible hearing gain

However this should not prevent the experienced otologist from per forming an explorative tympanotomy in such cases. Hearing gain was achieved in only one third of the cases published so far but increased know ledge of middle ear malformations was acquired in all cases.

ZUSAMMENFASSUNG

21 F lle von angeborenem M gel des ov len Fen ters sind bi heute beschrieben worden Es handelt ich ni ht um eine klinische Einheit. Mehrere Missbildungen sind öfters im Mittelohr zu finden Nur bei einem Drittel der Fälle wurde eine Hörverbesserung erreicht. Vier neue Fälle werd n beschrieben. Bei drei von diesen k men auch andere Körper Missbildungen or z. B. das Klippel Feil-Syndrom, Wolfsrachen und Facialis-Lähmung. Der Hörverlust war schwer aber einseitig in zw i Fällen. Tympanotomie zeigt in sämtlichen Fällen erschiedene M ssbildungen im Mitteloh auf, ausserdem Mangel des ovalen Fensters. Hörverbesserung wurde bei zwei Patienten erzielt, vorübergehend be einem und dauernd beim anderen. Einige embryologisch audiologisch und kophochirurgisch Probleme werden besprochen.

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(Reichert s cartilage) which is going to be the future tympanic part of the footplate but also from the *lateral capsular wall of the otocyst* ("lamina stapedialis" of the otic capsule) Subsequent fusion of the two layers and modification of the peripheral laminar tissue leads to the adult form of the stapes footplate surrounded by the annular ligament

If the aforementioned modification of the peripheral laminar tissue fails to appear or it is arrested no annular ligament will develop and the "lamina stapedialis will remain continuous with the surrounding capsular wall of the otocyst

It seems likely that slight degree of such developmental inhibition may lead to the so-called congenital footplate fixation affecting only the annular ligament (see House 1958) while a more pronounced inhibition—frequently associated with abnormal arcade—will lead to the anomaly here dealt with congenital absence of the oval window

Audiologically case No 3 is of particular interest Here the threshold of air-conduction was on the 85 dB level on both sides, while the bone-conduction threshold was on zero

First of all the extremely wide air-bone gap is remarkable in itself second it seems curious, that the *b-c* threshold is in fact on zero considering that both windows were lacking "The opinion is held widely that occlusion of both cochlear windows must necessarily reduce bone conduction responses to a severe degree This is thought to be so because of the resulting immobilization of the cochlear fluid" (Tonndorf 1966)

Consequently it has also been claimed that severe cases of otosclerosis are characterized by reduced bone conduction However Tonndorf's studies on the bone conduction in experimental occlusion of both cochlear windows have shown that the bone conduction in such experiments is only reduced by about 10–20 dB

In kopho-surgical respect the four cases here presented have been listed according to order of difficulty

In the first case with the Klippel Feil syndrome it could not be settled with certainty whether the auditory lesion was conductive or perceptive In addition the middle ear defects were exceedingly severe so in this case I desisted entirely from any attempt at performing kopho-surgery

In the second case no hearing improvement was obtained On the contrary the hearing deteriorated This can not be explained directly but it should be emphasized that it was impossible to examine the round window It is conceivable that the round window was not normal or not even present

In the third case a hearing gain was obtained it is true but it was lost again both after the first and the second operation, probably on account of osseous obliteration of the canal which had been drilled from the middle ear to the vestibule This is more likely to happen if such a canal is rather long as was the case here

In the last case, too a canal had to be drilled to the vestibule but as the

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EFFECT OF ENDOLYMPHATIC SAC ABLATION IN THE RABBIT AND CAT

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Tests of cochlea and vestibula function were carried ut two species of animals (6 cats and 15 rabbits) following which the left endolymph tl sa was removed in some with the remai ing being control animals. Subsequ t tests of function revealed depression of cochlea microphonics in both species with marked loss of vestibular function in the rabbit whil remaining ormal i the cat. Hist logic study re ealed there was mild cochlea hydrops in the cats and severe cochlear and vestibula hydrops in the rabbit which correlated to th loss f functio ted It th refore f llowed that th endolymphatic sa ablation was respo ible for the hydrops in both species and was most prominent in the rabbit in this short term experiment.

Guild (1927) presented the history of the discovery and subsequent theories of endolymphatic sac function and reported an experiment which suggested longitudinal flow of endolymph from the membranous labyrinth to the endolymphatic sac. Since Guild s first experimental work, many observations and experiments have been carried out to further the knowledge about the function of thi structure These observations have brought about a number of theories as to the role of the endolymphatic sac in endolymph circulation These theories may be summarized as follows

I. Th endolymphatic sac functions as an absorption site of endolymph in some species (Guild, 1927 Andersen, 1948 Engström & Hjorth, 1950 Altman & Waltner 1950 Dohlman & Ormerod, 1960 Lundquist *et al.*, 1963 Lundqui t, 1965 Kimura & Schuknecht, 1965)

II The endolymphatic sac functions as a secretory site of endolymph (Seymou 1954 1960)

III. Endolymphatic sac functi n is unnecessary for maintenance of inner ear function and histological cytoarchitecture (McNally 1926 Lindsay 1947 Lindsay *et al.*, 1952 Schuknecht & Kimura, 1953 van Egmond & Bri kman 1956 Schuknecht & Seifl, 1963)

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Asymmetries of head and body during posture and disturbances of right ing reflex and motor performances were observed Eye movements were recorded on an Offner Dynograph during optokinetic positional, caloric and rotatory tests. For these tests the animals were immobilized in an animal box.

The optokinetic test was carried out in cats by projecting an illuminated series of lines upon a black curved surface at a speed of 24 degrees per second. The optokinetic nystagmus to the right and left were recorded The derivation of these curves served as a calibration base for measuring the speed f the slow phase of nystagmus in caloric and rotatory tests. Since the rabbit did not follow the moving lines a different method for calibration was used One eye of the rabbit was di placed mechanically with a fine hook through an angle of 10 degrees From this data the speed of slow phase of nystagmus was then calculated

The positional tests were carried out in both a lighted room and total darkness. The eye movements were observed directly or with infra-red light and recorded while the animal was placed in erect right lateral, supine and left lateral positions.

The rotatory test was done by placing the immobilized animal upon a rotating device with the axis of rotation passing through the center of the head. In total darkness the animal was rotated first in anticlockwise direc tion and then after an interval of five minutes was rotated in clockwise direction The rotating device was accelerated at 25 degrees/sec until it reached an angular velocity of 120 degrees/sec. This was maintained for 80 seconds and then the device was decelerated at 25 degrees/sec² The data wa tabulated as t amplitude duration, total number of jerks, and speed f low phase of nystagmus when a positive response of at least five jerks was obtained

The caloric test w s done by pl cing the animal box on a stand with the horizontal canal in the vertical plane The test consi ted in irrigating for 40 second alternately th right and left ears, first with water at 28 C and then at 48 C. A five minute interval was paced between two consecutive irrig tions. If no response was obtained with either irrigation the ear was subsequently irrigated with water ranging between two and five degrees cent grade Th dat w tabulated as for the rotatory test

T sting of cochlea function

The anim l without anesthesia was placed in the fixation box situated w th the left ear t a distance of two centimeters from a calibrated l ud-speaker The stim lu consisted of pure sine waves of frequencies varying n oct es from 125 cps to 8000 cps. Th cochlear microphonic response wa recorded on standard equipment consisting of a preamplifier filters, and oscilloscope The magnitude of the output was measured peak-to-peak d plotted a function of the input The input-output curves of cochlear microphonics w re determined in three cats and ten rabbits.

IX The endolymphatic sac functions as a pressure regulator (Allen, 1964 Lawrence 1965 House 1954 House 1966 Simmons & Mongeon 1967)

From the above tabulation it is clear that there are discrepancies among some investigators as to the function of the endolymphatic sac. Some of the disagreement may arise from the comparison of experimental data which has been obtained from different species (rabbit cat monkey man, guinea pig) The function of endolymphatic sac may have species differences as suggested by Kimura & Schuknecht (1965) They noted hydrops in the guinea pig following endolymphatic sac destruction this being contrary to the findings of Lindsay (1947) who was unable to find a histological change after similar endolymphatic sac destruction in the monkey

The purpose of this experiment was to further explore the suggestion of Kimura and Schuknecht regarding species differences as to the endolymphatic sac function

METHODS

Surgical procedure

Six healthy adult cats and 21 young Deutch rabbits were anesthetized intraperitoneally with 30 mg/kg sodium pentobarbital Permanent steel electrodes in the cat and silver wire electrodes in the rabbit were implanted in the outer canthi of the orbits and middle of the forehead as terminals for electronystagmographic recordings After implanting the electrodes, or in some cases at a second operation a silver wire electrode was placed in the scala tympani of the left ear via the round window Several days following surgery control tests of vestibular and cochlear function were carried out Surgery was then performed for removal of the left endolymphatic sac

In the cat a lateral incision was made along the left lamboidal suture line The dissection was then carried out extradurally to exposure of the left endolymphatic sac in its fossa in the temporal bone in apposition to the sigmoid sinus The sac was removed surgically and the tip of the duct was cauterized for two to five seconds with the cautery set at a level where it stimulated bud didn t burn the exposed neck muscles, as seen under a dissecting microscope The wound was packed with Gelfoam and closed with chromic sutures

In the rabbit the endolymphatic sac was approached through a posterior occipital midline incision The left occipital bone was removed to the lamboidal suture which in turn was drilled down until the sigmoid sinus was clearly visible Then without penetration of the dura the endolymphatic sac was cauterized and the wound closed

Testing of vestibular function

This function was tested in all animals before and at least every ten days following ablation of the endolymphatic sac

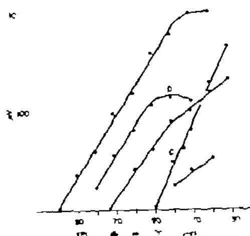


Fig. 1 The input-output functions of the cochlea microphonic measured peak-to-peak are displ yed f ne frequency (4000 cps) during the nimal' lif A is control, B four day following surgery C 15 days, D 23 day nd F 63 days. There ppears t be fluctuation of the output between 2.5 nd 50%

ward th left of the animal from the right lateral and supine positions while from the left lateral position, there was an under-turning.

Conjugate deviation of th eyes was noted in the nine abnormal rabbits with the left eye rolled-up and the right one down Strong spontaneous nystagmus noted in five of the animals, for as long a 20 days following endolymphatic sac surgery increased in intensity with chang of the head position The spontaneous nystagmu was vertical downward in the left eye and vertical upward in the right eye in three animals. Two animals ex hibited horizontal nystagmus to the left. The spontaneous nystagmus was observed in the light f r 10 days in on animal having subsided earlier in the thers. On the ther hand this nystagmus was clearly observed in darkness f r as long as 25 days in one animal.

The rabbit used in this experiment were difficult to test with rotatory and caloric stimuli due to their tendency to attain a catatonic stat when placed in the holding box. Although alert, even in the unoperated state, the animals would ften f ll to respond, as shown in Table I Though the above difficulty occurred, responses to rotation were found to be reduced in the test situation after operation On the other hand th results of the caloric test displayed a significant lack of response when the left ear was stim l ted

The input-output curves for cochlear microphonics were reduced in seven rabbits and fluctuated between 2.5 and 50% of the control measure ment (Fig 1) In two there were no responses to sound stimuli

Seven of ten rabbit were uitable for complete study and were sacrificed t varying times following the surgery three early (9 10 and 32 days) and

TABLE 1 Vestibular responses* to caloric stimuli before and after removal of the left endolymphatic sac in rabbits

Pre-operation	Left ear post-operation Yes	Left ear post-operation No	Right ear post-operation Yes	Right ear post-operation No
Yes	1	9	7	4
No	1	1	1	0

The charts f r th right and left ars are dissimilar at a 99+ % level

Histological studies

All the animals were sacrificed under sodium pentobarbital anesthesia For fixation intravital perfusion with Heidenhainsusa was used The temporal bones cerebellum and brain stem were removed in one block nd processed for histopathological studies Serial sections for each animal were stained with hematoxylin-eosin

RESULTS

1 *Rabbits*

A group of five rabbits served as controls. In all these animals cochlear electrodes were implanted Vestibular function tests were unaltered in all five and four had good cochlear function No cochlear output could be measured in one Histologic study revealed an inner ear like that of the control side in four animals with the sigmoid sinus being compressed in two The animal that lacked cochlear function was found to have moderate outer hair cell loss a cell covered atrophic tectorial membrane and severe atrophy of the stria vascularis without hydrops No abnormalities were found in the vestibular system in any of the animals.

The experimental group of 10 animals had the left endolymphatic sac removed and the endolymphatic duct destroyed by electro-cautery In five rabbits, the cochlear input–output function curves were determined as well as the vestibular function Vestibular upset occurred in nine animals either immediately or within a five to nine day period following surgery Motor function assessment revealed a rotation of the head so that the left ear was underneath in nine animals. This rotation was manifest one to nine days following surgery and persisted until the animals were sacrificed Coincident with the onset of head rotation a circling locomotion to the left was observed This persisted for 20 days in two animals. Following this the animals could locomote on a straight line Inability to perform the righting reflex tests appeared at about the same time as head rotation and persisted until sacrifice. Disturbance of the righting reflex consisted of over turning to-

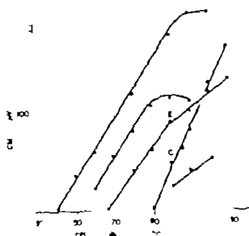


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Fig 2. A ph t mi rograph f th blocked nd lymph ti duct (a) New bone i seen (ar w) i th re wh re d lymph tic sa w pplied t th igm id in ( ) (B) The ight id at th sam le l d monstrating th e d l mphatic d ct (d) and s ( ) rel ti n hip to the igm id inu ( ) petrosal l be f th parafloc lu (h) and th poste i semi rcul nal ( ) H & E stai Th m k r i eq l t 1 mm

four later at (66 70 71 and 80 days) Three animals were unsuitable one died and was not perfused and two had purulent otitis media and labyrinthitis

The animal with normal vestibular function having been sacrificed at 70 days following surgery was found to have a minimal destruction of the endolymphatic sac and a mild hydrops of the saccule and cochlear duct The remaining six rabbits all were found to have complete left endolymphatic sac destruction (Fig 2) and marked cochlear duct and saccule

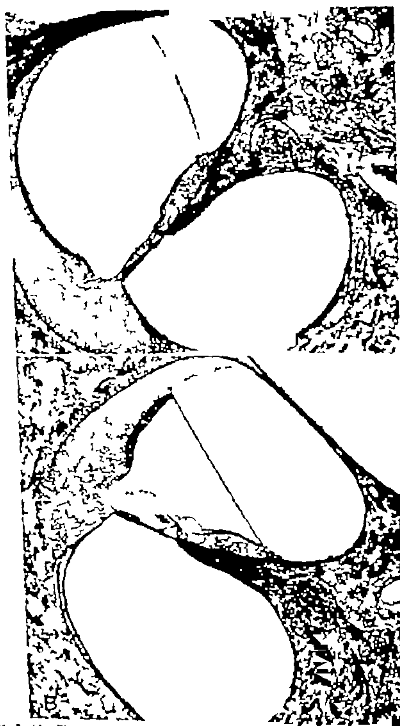


Fig. 3 (A Photomicrograph of the left basal coil showing cochlear duct hydrops, sl[ight a]trophy compression of the organ [o]f Corti, external hair cell loss [a]nd preserva[tion] of neural [e]lements. (B) The basal coil of the unoperated right [s]ide [a]t [a]ppro[x]imat[e]ly the same le[ve]l for comparison. H & E stain. The marker [is] equal [to] 1 mm.



FIG. 2. A photomicrograph of the blocked d l mph t duct ( ) \ w bo l seen (arr ms) n th rea wh re end l mph tic sa w pplied t the lgm id lnu ( ) (B) Th right d t the same l l dem n trating th nd l mphatic duct (d) a d sa (l tl hlp t th sigm id lnu ( ) petrosal l be f the paraflocculu (h) and th post l seml lrcul l ( ) H & F stain Th m k l eq l to 1 mm.

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Fig. 6. A Photomicrograph of pical coil f [illegible] imal sacrificed t 10 days about g mild hydrops, marked strial atroph la of one organ of Corti with preserv tion of the other nd striking los of neural lements. New bone is noted i the spiral ligament of one coil. B The unoperated right ea for comparison. H & E tain. The marker is equal t 1 mm.



Fig. 4 (A) Ph tomicrog ph f th sacc l pe t d h w g m rked h drops as n ted when thi l compa d t th u perated t the same lev l (B) H & E tal The ma ker is eq al to 1 mm



Fig. 8. A. Photomicrograph of apical coil of an animal sacrificed at 70 days showing mild hydrops, marked strial atrophy, loss of one organ of Corti with preservation of the other, and striking loss of neural elements. New bone is noted in the spiral ligament of one coil. (B) The unoperated right ear for comparison. H & E stain. The marker is equal to 1 mm.



F G. 6 (A) Photomicrograph of the cochl of the l ft ea of cat sh wi g cochlear duct hydrops with ut changes. (B) Th un perated ad at ppro imat l the same level f comparison H & E stai Th m k l equal to 1 mm

hydrops (Figs 3 and 4) Along with the hydrops changes were noted in the epithelial and neural structures associated with the cochlear duct (Fig 5)

In the three animals sacrificed early there were several findings which were not evident in the three animals sacrificed later With early sacrifice there was a marked dilatation of stria vessels, red blood cells in the cochlear and vestibular perilymphatic spaces and few changes in the organ of Corti or neural elements With late sacrifice there was flattening of the organ of Corti along with some apical and middle coil outer hair cell loss coincident with nerve fiber and ganglion cell loss (Figs 3 and 5) New bone formation was evident in the scala vestibuli in the apical region and in



FIG. 6 ( ).

the perilymphatic spaces of the posterior canals. The changes as men tioned ppeared to be un elated to the presence f the cochlear electrode n the experimental animals as those were not seen in the control animals

2 *Cats*

Tw f the six cats had abnormal locomotion with left lateral pulsion during the first 10 days following surgery These same two animals had righting difficulty with over turning from the supine and left lateral position for 40 days following surgery One animal had a spontaneous nystag mus toward the operated side for two days after surgery While in total darkness, this animal along with three others, had a direction changing, f tigable positional nystagmu as noted on infra-red obser tion and the lectronyst gmographic recording In two animals thi wa noted for four



FIG. 6 (A) Ph t micrograph f th cochlea of tl left ea f t h wing cochlear duct hydrops with nt hanges. (B) The un perated sid t ppro lmat ly th same level for comparison H & E t l Th m k l equal t 1 mm

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Abnehmen der cochleären Mikrophonie im Kaninch n mit einem deutlichen Verlust der vestibularen Funktion welche in der Katz normal blieb Die histologische Untersuchung zeigt in den Katzen einen mittelcochleären Hydrops und in d n Kaninchen einen estibularen Hydrops, di beide mit dem festgestellten Funktionsverlust k rrelierten. Daher kan der Schluss gezogen werd n, dass in beiden Spezies die Entfernung des endolymphatischen Sackes für die Hydrops verantwortlich war und dass es während dieses kurzfristige Experimentes in Kaninche am deutlichsten erschie

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days while it persisted some 25 days in the others. The rotatory and caloric tests were unchanged in five cats. One cat developed a canal paresis on the operated side which was persistent to the time of sacrifice at 60 days.

The input–output functions of cochlear microphonics were reduced in two animals to approximately 15% of the control while the input–output remained at control levels in the remaining one

Observation of the serially sectioned temporal bones showed that the endolymphatic sac and duct had been destroyed in five of the six cats. In the remaining cat the inner ear appeared as on the control side

The pathology noted in the successfully operated cats was mild cochlear duct hydrops (Fig 6) The contents of the cochlear duct the hair cells, supporting cells, pillar cells stria vascularis, and neural elements appeared as on the control side in the five animals Careful examination of the saccule utricle and semicircular canals in all the cats including the animal with the horizontal canal paresis failed to disclose any abnormalities

DISCUSSION

Nabeya (1923) pointed out that the whole vestibular apparatus in the rabbit was drained by the vestibular vein which lies adjacent to the endolymphatic duct This vein was destroyed in the above rabbits In reference to the work of Kimura & Perlman (1956) and Perlman (1966) it probably gave rise to the early perilymphatic hemorrhage and late new bone formation but not the hydrops

The hydrops was not secondary to acute infection and probably was not due to serious labyrinthitis created through the use of cautery For when cautery of much greater magnitude was used directly within the otic capsule by Schlander (1948) and Shall & Rambo (1948) consistent development of hydrops was not found

The relative lack of vestibular abnormalities in the cats with demonstrated physical and histologic cochlear abnormality possibly reflects the inability to critically test this system In the rabbits the gradual development of severe vestibular lesions due to the pronounced hydrops and venous occlusion was easily demonstrated in routine vestibular tests

The degree of hydrops in the rabbit would seem to indicate that the endolymphatic sac is more important for endolymph equilibrium than in the cat

ZUSAMMENFASSUNG

An zwei Tierspezies (6 Katzen und 15 Kaninchen) wurden Tests der cochleären und vestibulären Funktion durchgeführt und in einigen Tieren wurde lansel der linke endolymphatische Sack entfernt während die restlichen Tiere als Kontrolltiere dienten Darauffolgende Funktionsteste zeigten in beiden Spezies ein

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Choice of Cases

In the course of ten months we collected 30 cases of unilateral tenderness of the tip of the greater hyoid cornu and examined them clinically and radiologically The patients treated were 13 men and 17 women between 30 and 60 years of age with an almost uniform age distribution over these three decades Only one female patient aged 20 was appreciably younger The subjective symptoms reported closely resembled the concomitant manifestations of an elongated styloid process and largely coincided with the symptoms described by many workers constant piercing pain laterally in the pharynx spreading to the ear sensation of foreign body on dry swallowing difficulties of swallowing and feeling of pressure in the neck

Symptoms

In these cases compiled on the basis of tenderness in the hyoid arch some important deviations from the classical Eagle syndrome brought to light by close examination In six patients the disturbances appeared before tonsillectomy or such operation had never taken place In only four cases was it possible to establish elongation of the styloid process In two cases there was calcification of the stylohyoid ligament In all the others the X ray picture showed no changes in the organs of the second pharyngeal arch

A striking feature was the constancy of the pain over the years and its exacerbation on stretching the muscles lying between the hyoid and the styloid process by turning or inclining the head to the affected side a circumstance which put us on to the cause of the pathological picture Sticking out the tongue occasionally produced painful sensations The tenderness of the tip of the greater hyoid cornu was repeatedly associated with palpable thickening of this part of the bone The spontaneous pain immediately abated in four cases on raising the hyoid cornu Often there was *also some tenderness of the styloid process but this could not always be* verified since the process, if not elongated or displaced, cannot be readily palpated either from the external surface or the inferior tonsillar pole In the event of tenderness of the hyoid however the palpating finger always elicited a reaction similar to the spontaneous pain

A further symptom seen in six patients was mild but persistent hoarseness and in two cases thickening of the parotid gland on the same side The general status showed nothing of particular note raised temperature and accelerated ESR were absent as were also changes in the blood picture

Etiology

Of embryological significance is the descensus laryngis (Wustrow 1966) The primary laryngotracheal skeleton as we know it in amphibians at



Fig. 1 Elongated styloid process on the right side

first comes into contact with the hyoid bone by an oral shift In nearly all mammal the larynx is situated very high, dorsal to the hyoid, and is kept in thi position by a strong synchondrotic union between larynx, hyoid and the base of the skull (Jordan, 1962) In anthropoids and, parti

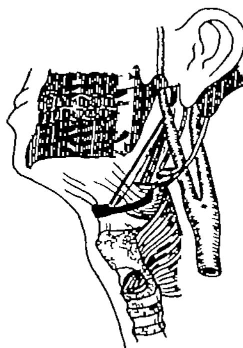


Fig. 2 Calcified stylohy id lig ment on the right side



FIG. 3 Normal X ray picture T ndernes of hyoid bon

cularly in man a caudally directed displacement of the larynx beneath the hyoid then occurs secondarily resulting in the appearance of the mesopharynx. The cartilaginous-osseous connection is replaced by a ligamentous-muscular suspensory apparatus (Fig 4) Taking an important part in this



F g 4 Su pensi n f th lary

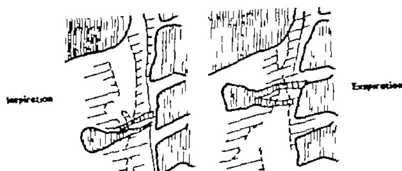


Fig. 5. Movement of hy id d ri g respiration.

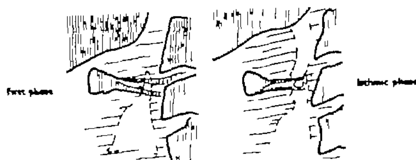


Fig. 6. Movements f hy id d ring sw llowing.



Fig. 7 Moveme t of hy id duri g phonation.

m bile pen ion f the larynx are the formations which orginate from the second nd third pharyngeal arches. From Reichert s cartilage are for med th tyloid process, the lesser horn of the hyoid and the interposed ligamentum tylohyoideum already undergoing *in ut ro* connective tissue transf rmation (M cucci, 19J9) Second ry ossification of this ligament n the postn tal period are very frequent and it is still an open question whether it contain formed centres f os ification (van Spee 1930) or whether it i a matter of maintenance of osteogenetic powers (Le Double

1903) The superior point of insertion of the ligament ossifies at birth (Marcucci 1959) the inferior (upper part of the hyoid) a few years later The ossification of the rest of the hyoid stemming from the third pharyngeal arch also occurs after birth The postnatal growth in length of the neck allows the hyoid in the course of the descensus laryngis to descend to its final position However the ossification of the hyoid and styloid process is at this stage not yet completed so imposing a strain on the suspensory apparatus of the hyoid before the final state is reached

The hyoid fixed only by ligaments and muscles, on respiration swallowing and phonation (Figs 5–7) performs distinct movements essentially of the character of a rocking motion with the central insertion of the digastric muscle as hypomochlion The body of the hyoid rises on exspiration, particularly with the glottis closed and falls in inspiration It also descends on swallowing at the end of the isthmic phase when the tongue on contraction of the mylohyoid styloglossus and hyoglossus muscles arches posteriorly and superiorly and the chyme passes the isthmus fauci (Marcucci 1959) Similar displacements are observed in intonation of certain sounds. For O the hyoid is lower than for Q The muscular insertions at the greater horn of the hyoid are thus exposed to varied and persistent mechanical stresses.

Pathogenesis

Having regard to these anatomical and physiological bases, it is logical to think of degenerative and inflammatory phenomena which develop in other narrow bone projections bearing muscle insertions described as "insertion tendinosis" The classical example of this is epicondylitis humeri. Such forms of apophysitis may however appear in all muscle insertions with a narrow base Thus, they are also found in the transverse processes of the cervical and lumbar vertebrae (Belart 1957) Fahlgren *et al* (1966) have described acute tendinitis of the long muscle of the neck with inflammatory phenomena at its insertion with the atlas. The cause of these symptoms lies in the special histological structure At the tip of such bone projections the tendon fibres of the inserting muscle do not connect with the periostium possibly torn off on contraction but run into the bone The point of insertion is lined with an external noncalcified and an internal calcified cartilaginous layer (Fig 8) which on change in the direction of pull of the muscle have the task of lessening the deleterious inflexion of the tendon fibres at the point of entry into the bone (Schneider 1959) At no other point of their total course have the tendon fibres to take up such heavy tensile and compressive stresses The mechanical stress on the tendon anchorage reaches its peak on change in the angle of insertion consequent on the described displacements of the hyoid

The strikingly low metabolism of tendon tissue is out of proportion to it work load Thus soon after the age of 25 years wear lesions develop (Stucke 1950) The main site of the degenerative changes is the zone of insertion of

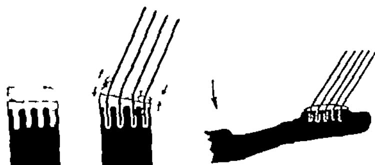


Fig. 8. Tendon insertion i narrow bone processus.

the tend n into the bone and the directly adjacent tendon segment. Since the structural make-up of the insertion zone matches that of the joints, the degenerative transformations in the tendon insertion closely resemble those in arthrosi deformans (Glatthaar 1944) The first histological find ings came from Sandstrom & Wahlgreen (1937) They were confirmed by many workers, in particular Pedersen & Key (1951) on the basis of excised pecimens. The ageing of connective tissue begins with precipitate forma tion in the ground substance (Schallock & Linder 1957) Then follows welling and shrivelling of the tendon fibres with desintegration of the fine tructure (Schoer 1936) This, in turn is followed by fatty degeneration formation of foci of necrosis and finally promoted by the appearance of hyalin by deposition f calcium. The nerve end organs lying in the tendon are irritated by the increased tissue pressure and the pathological deposits. Muscul r contr ction or palpation of the affected tendon area produce pain Later even without tendon strain, there is a persistent sensation of pain and reflex restriction of movement.

Predisposing factors in the genesi of insertion t ndinosis are congenital incompetence of the tissue excessive strain and traumata In the presence of a locu minori resistentiae thus created, disturbances in blood flow general or focal infections and lso irritations of the corresponding nerve path m y engender the clinical picture Vegetative and hormonal distur ba ces, n tably hyperthyr idism, may also be causally implicated

Di gnosis

W t rn t n clinical findings (see Table 1) and summing up we may say that ll tl e prerequi ites f r the onset of insertion tendinosis are present In th hy id an l lso in the styl id process we have muscl inser tion w th a narr w base which re exposed t heavy and regular mechani l tresses. The ul jecti e manifestations meet the criteria of apophysiti t tained pain t rest thi kening nd tenderness of the affected bone pro ces nd typic l pain on st etching th muscles (called Zerrschmerz" by

Belart 1957) Hoarseness occasionally observed is possibly a consequence of limitation of movement of the hyoid The age distribution of our cases tallies well with the findings of Schneider (19ɔ9) on tendopathies in the shoulder and arm region

Treatment

In treating the patient we paid due heed to the experience of the rheumatologist Immobilization of the affected tendon insertions was not possible in the cases selected by us Heat applications have to be used with some circumspection All the same our patients took kindly to heat in all forms. In one case a change of climate to a warm country had a beneficial effect

TABLE 1

Name	Sex	Age	Hyoid tenderness	Styloid proc symptoms	Hoarseness	Parotid swelling	Tonsils removed	Elongated styloid process	Calcification stylo y ld ligam nt	X ray picture	Result (t lmpl tol)	Cervical syndrom
H. H.		20	+	+			+			Norm	+	
M B	♀	35	+	+			+			Norm		
N M.	¥	3?	+	+	h		+	Elong.			+	
H. S	ɔ	34	+				+			Norm	+	
G B	♀	39	+	+			+			Norm	┴	
M N	¥	30	+	+	h		+		C		+	
E. A	o	36	+				+			Norm	┬	
B M.		34	+	+			+			Norm		
F W		44	+	+	h		+			Norm	+	
P S	¥	47	+	+	h		+	El ng.			*Op*	
P K		45	+	+			+	El ng.			+	
A. S.	o	49	+	+			+			Norm	+ +	CS
N M		41	+			P	+			Norm	+ +	CS
R. O		46	+	+			+			Norm	+ +	
L. S		46	+	+						Norm	+	
H. R		45	+	+			+			Norm		
F R.		51	+	+		P			C		+	
A H		59	+	+	h		+			Norm	+ ┴	CS
A. S		58	+	┬			+			Norm		
J P		4	+	+						Norm	┴	
F W		51	+							N rm		
A L.		9	+		h					Norm		CS
D M.		9	+	+			+	Elong			+ Op	
A. K.		1	+							Norm		
R. M.		50	−	+			+			Norm	+	
D W	¥	44	−	+			+			Norm	+	
G B.	¥	39	+	+			+			N rm	+	
A. B.	♀	31	+				+			Norm	+ +	
C S	o	42	+	+						Norm	−	
M H.	♀	45	+	+			+			Norm		

on the symptoms. Rapid relief of the pain can often be observed on passing galvanic current through the affected region. The pathological state of irritation of the sensitive nerves is thereby mitigated and the superficial, and also deeper vessels dilate. Histamine iontophoresis reinforces the favourable effects of tissue hyperaemia but for external reasons we employed it only twice and then with only temporary success. Radiation treatment and sonication were not used.

The agent of choice is local infiltration of procaine combined with Claudden, acetylcholine or even better cortisone derivatives. The local anaesthesia applied to the affected bone process often causes sudden, though mostly temporary disappearance of the pain. In contrast, injections of physiological saline tried by us had no effect. Cortisone is just as suitable for the treatment of insertion tendinosis as it is for arthropathia deformans, exerting as it does an inhibitory effect on mesenchymal reactions. It also helps to reduce the swelling of the tissues and at the same time thereby acts as an analgesic. After various attempts we finally turned to the less dangerous Impletol in which the pain-relieving effect of procaine is considerably enhanced by the caffein added (Seyffarth, 19 7). We have also with time modified the technique of injection. At the hyoid it is not always easy to find the desired site with the injection needle and this is much more difficult in the styloid process. Moreover the path to this point runs by large vessels and nerves and proves to be highly painful. Finally we adopted the procedure of infiltrating the lower pole of the tonsillar niche with Impletol and also the adjoining region of the palatine arch. This gave dramatic effects. In 20 patients persistent freedom from disturbance was achieved with 1–3 injections. In five the effect appeared suddenly immediately after ending the injection (Sekundenphänomen Hunecke). In two patients the symptoms were present after treatment but in minimal form. In two other female patients an elongated styloid process had to be shortened surgically with cure in one but with recurrence in the other of the old neuralgiform complaints a few months after the intervention. They finally vanished on injection of Impletol. This form of treatment thus appears promising.

ZUSAMMENFASSUNG

An Hand von 20 Patienten wird gezeigt, dass sich unter den verschiedenen Arten von Halsbeschwerden ein bestimmtes klinisches Bild abgrenzen lässt, dessen als gemeinsames Merkmal ein ausgeprägter einseitiger Druckschmerz über der Spitze des grossen Zungenbeinhornes und zeitweilig auch über dem entsprechenden Processus styloideus ... ist. Im Vordergrund steht ein konstanter über Jahre dauernder Halsschmerz, welcher ins Ohr ausstrahlt und mit Druckgefühl im Hals, mit Schluckhemmung und mit gelegentlicher Heiserkeit verbunden ist. Beim Kopfdrehen und Schlucken tritt ein typischer Zerrschmerz auf. Nur in 4 Fällen liessen sich palpatorisch und röntgenologisch ein verlängerter Processus styloideus nachweisen, 2mal lag eine Verkalkung des Ligamentum stylohyoideum

Es werden Ätiologie und Pathogenese dieser Erkrankung besprochen. In Analogie zu ähnlichen Erscheinungen an schmalen Knochenvorsprüngen der Extremitäten und der Wirbelsäule wird das Vorliegen einer Insertionstendinose angenommen. Es sind dies degenerativ-entzündliche Vorgänge im Sehnenanteil schmalbasiger Muskelansätze unmittelbar an ihrer Verankerung im Knochen. Die Therapie stützt sich hauptsächlich auf Wärmeapplikation, Histaminjontophorese und auf lokale Infiltration von Anästhetika in Kombination mit Cortison. Als besonders wirkungsvoll erwiesen sich Impletolinjektionen an der Basis der Tonsillarnische.

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INFLUENCE DE L'ÉLIMINATION DES UTRICULES SUR LES RÉACTIONS DUES À LA STIMULATION DES CANAUX SEMI-CIRCULAIRES HORIZONTAUX CHEZ LA GRENOUILLE

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On étudie chez la Grenouille privée de la vue par la section des nerfs optiques, les réactions vestibulaires postrotatoires (réactions dues à la stimulation des canaux semi-circulaires horizontaux) avant et après section des nerfs utriculaires. Pour une même vitesse de rotation les réactions observées à l'arrêt sont plus faibles chez une grenouille privée des deux utricules que chez une grenouille seulement aveugle. Cependant, les canaux semi-circulaires horizontaux sont intacts ainsi que leurs nerfs ampullaires, et les crêtes, à l'examen histologique apparaissent normales. On en conclut que la perte des utricules affaiblit les réactions dues à la stimulation des canaux horizontaux. Cet affaiblissement est plus ou moins important selon les individus, et même inexistant chez quelques-uns.

Des expériences faites par McNally (1931), McNally & Tait (1925, 1933), Tait & McNally (1934), Van Eyck (1960) relatent le comportement d'animaux après élimination fonctionnelle de tel ou tel récepteur vestibulaire. Des travaux d'électrophysiologie sur les Poissons (Katsuki *et al.* 1954, Löwenstein & Sand, 1940, Löwenstein 1956), la Grenouille (Ross, 1936, Ledoux, 1949, 1954, 1958), le Pigeon (Van Eyck, 1951), le Chat (Adrian, 1943) ont montré que tous les organes vestibulaires présentent une activité spontanée qui est augmentée ou inhibée suivant le sens de déflexion de la cupule (pour les canaux semi-circulaires) ou le degré d'inclinaison de la tête (pour les utricules). Aucun travail n'a été fait en vue de considérer si l'élimination fonctionnelle d'un organe vestibulaire avait une influence sur les réflexes ayant pour origine d'autres récepteurs du vestibule. Tait & McNally (1934) remarquent seulement que la section des deux nerfs utriculaires chez la Grenouille abolit les réactions à la gravité et modifie les réactions de l'animal soumis à une rotation autour d'un axe vertical. Mais ces auteurs n'indiquent pas si les réactions spécifiques dues à la stimulation des canaux horizontaux sont modifiées. Van Eyck (1960) au contraire précise que les réactions vestibulaires rotatoires restent sensiblement normales après destruction d'un utricule chez le Pigeon.

Es werden Ätiologie und Pathogenese dieser Erkrankung besprochen. In Analogie zu ähnlichen Erscheinungen an schmalen Knochenvorsprüngen der Extremitäten und der Wirbelsäule wird das Vorliegen einer Insertionstendinose angenommen Es sind dies degenerativ-entzündliche Vorgänge im Sehnenanteil schmalbasiger Muskelansätze unmittelbar an ihrer Verankerung im Knochen Die Therapie stützt sich hauptsächlich auf Wärmeapplikation Histaminjontophorese und auf lokale Infiltration von Anästhetika in Kombination mit Cortison Als besonders wirkungsvoll erwiesen sich Impletolinjektionen an der Basis der Tonsillarnische

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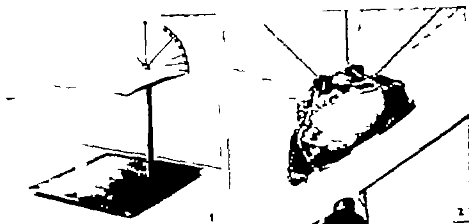


Fig. 1 Appareil utilisé pour incliner la grenouill

Fig. 2. Réactions compensatrices d' ne grenouille sur l plateau incliné de 35 ers l droit On oit qu'il existe, entre le ni ea des 2 yeux, une différence d'un interligne (5 mm) mesurée su le rapporteur

rotation. I pparell de stimulation rotatoire a déja été décrit par Gribenskl (1964)

d'autre part, le plan supportant l animal a été incliné vers l avant et vers l'arrière vers la droite et vers la gauche Les réactions compensatrices ont été observées ur un plateau rectangulaire inclinable autour d un axe horizontal La grenouille est posée sur ce plateau de façon que sa tête soit ituée sur l'axe de rotation du plateau, et l'on peut basculer l animal, selon sa position, vers l avant et vers l arrière ou bien vers la droite et vers la gauche

Un rapporteur dont le diamètre est égal à la largeur du plateau est fixé ur l'un des montant verticaux de ce plateau Le rapporteur est divisé en l gnes parallèles à son diamètre espacées les unes des autres par des inter alles le 5 mm (Fig. 1) Lorsque le plateau est incliné vers la droite par xemple la grenouille penche du côté gauche de façon à compenser l'incli n ison du upport Mais la tête de la gren uille ne conserve pas une horizontalité parfaite et même lorsque les réaction compensatrices sont excellen tes, l' nimal reste faiblement incliné du côté droit Les yeux, qui ont été hoi is comme reperes en raison de leur position proéminent sont situés à des ni eaux différents, le gauche ét nt plus haut que l droit. Lorsque la l ff re ce de nive u entre les deux veux tt int 5 mm on n te la valeur en degrés, de l'inclinaison du pl teau (Fig 2)

S cett différence de mm que l on observ entre les deux yeux n est tteint que pou un al ur import nt de l'inclinaison, les réaction compensatrices sont bonnes Si, au contraire elle est atteint pou une faible leur le l'inclinaison, les réaction compensatrices sont faibles.

Le pl teau d it êtr incliné très lentement et san à-coups de f con à obtenir des ép nses utricul ires u l pures qu possible en élimin nt toute stimulation des can ux semi-ci culaires verticaux.

Le présent travail a été entrepris dans le but de savoir si la suppression des utricules modifie les réactions dues à la stimulation des canaux semi circulaires horizontaux

MATÉRIEL ET TECHNIQUES

L élimination fonctionnelle des deux utricules a été réalisée en sectionnant les nerfs utriculaires à l aide d un fin crochet à bords tranchants. L ouver ture de la capsule labyrinthique et la section des nerfs ont été faites sous microscope opératoire Zeiss

Le nerf utriculaire est formé de fibres issues de la branche antérieure du nerf vestibulaire Cette branche antérieure se ramifie à la face ventrale du labyrinthe et *donne naissance à une première ramification le nerf saccu* laire Elle passe alors à la surface de l utricule et se divise ensuite en deux branches qui innervent l une la crête ampullaire du canal horizontal, l autre la crête ampullaire du canal vertical antérieur Les fibres qui vont innerver la macule utriculaire se séparent donc de la branche antérieure du nerf vestibulaire à sa face dorsale entre la ramification sacculaire et la rami fication qui donne naissance aux deux nerfs ampullaires. Ces fibres s étalent en éventail sur la macule utriculaire

La section du nerf utriculaire est une opération délicate Nous avons procédé de la façon suivante le crochet à bords tranchants est glissé sous la branche antérieure du nerf vestibulaire entre la face dorsale de cette grosse branche nerveuse et la face ventrale de l utricule, du côté interne de la capsule labyrinthique juste après la ramification sacculaire Le crochet dont l extrémité recourbée est d une longueur très peu supérieure au diamètre de la branche antérieure du nerf vestibulaire est alors tiré doucement vers l avant en direction des ampoules des canaux horizontal et vertical antérieur puis vers l arrière et ainsi de suite plusieurs fois Les fibres sont ainsi coupées et pour essayer d éviter leur régénération il est possible de glisser un minuscule carré de papier entre la branche antérieure du nerf vestibulaire et l utricule

Trente grenouilles privées de la vue par section des nerfs optiques (Cas ton & Gribenski 1965) ont subi la section des deux nerfs utriculaires Elles ont été étudiées le lendemain de l opération puis une semaine plus tard Certaines d entre elles ont ensuite été examinées toutes les semaines pen dant 1 ou 2 mois, d autres ne l ont été que tous les mois pendant 2, 3 ou 4 mois Un certain nombre de ces animaux avaient été étudiés aveugles avant la section des nerfs utriculaires A chaque étude les animaux ont été soumis aux tests suivants

d une part des rotations dans le plan horizontal aux vitesses uniformes de 120 60 30 15 8 /s dans les deux sens Ces rotations ont duré 3 minutes aux vitesses de 120 et 60 /s., 1 minute aux autres vitesses, de façon que l appareil vestibulaire soit revenu au repos au moment de l arrêt (Griben ski 1964) Les réactions à l arrêt ont été notées pour les deux sens de

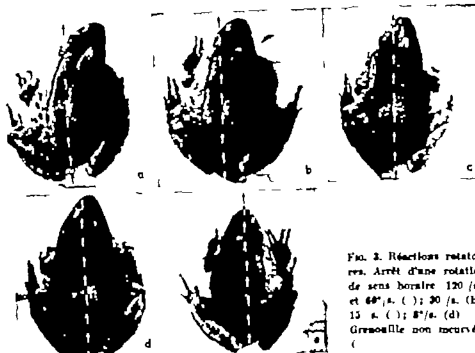


FIG. 3. Réactions rotatoires. Arrêt d'une rotatio de sens horaire 120 /s. et 60°/s. ( ); 30 /s. (b) 15 s. ( ); 8°/s. (d) Grenouille non incurvée (

b) *Réactions à l'arrêt d'une rotation de sens horaire* (A de rares exceptions près, les réactions observées à l arrêt pour les 2 sens de rotation sont d' mplitude égale pour une même vitesse de rotation du plateau)

Vite e 120 s. Au lendemain de l opération les réactions postrotatoires dirigées vers la droite sont très variables d une grenouille à une autre Chez 2 animaux les réaction ne sont pa modifiées, tandis que 28 grenouilles ont des réactions affaiblies par rapport à celles qu elles présentaient avant l operation 18 d'entre elles s'incurvent faiblement ou très faiblement vers la droite 4 autres gren uilles n effectuent qu un faible mouvement de tête ers la droit *ce mou em nt n affecte pas la ymétrie de l animal) et par f i* il ne se produit même aucun m uvement appréciable 6 animaux incurv nt moyennement ers la droite

60 Parm les 28 gren uilles d nt les réactions postrot toires ont été modifiées par l section les nerf utriculaires, 17 animaux s'incurvent f iblement ou très f iblement vers la droite 8 autres n effectuent qu un f ibl m u ment de t te qui n affecte pa la ymétrie de l animal ou bien ne présent nt même ucune réaction, et 3 incurvent moyennement vers la droite

30 s. 16 grenouilles 'incurvent faiblement ou très faiblement vers la d oite t rs que 12 animaux ne présentent ucune réaction ou bien n effec tuent qu un très léger mouvement de têt vers la droit

RÉSULTATS

1) *Etude d'une grenouille seulement aveugle*

a) Réactions à l'inclinaison vers la droite et vers la gauche Lorsqu on incline le plateau vers la droite la tête de l animal par des mouvements saccadés se penche du côté gauche et tend à conserver une position sensiblement horizontale Lorsque l amplitude de l'inclinaison devient importante (40 environ) le bras droit s étend latéralement alors que le bras gauche se colle tout contre le corps de l animal Pour une même grenouille les réactions à l inclinaison vers la gauche sont symétriques des précédentes et d amplitude égale On ne note pas de différences sensibles dans l amplitude des réactions compensatrices lorsqu on étudie la grenouille à plusieurs jours d intervalle mais d un animal à l autre cette amplitude peut varier considérablement

b) Réactions à l arrêt d une rotation dans le plan horizontal (Les réactions sont symétriques pour les deux sens de rotation et leur amplitude est égale pour une même vitesse de rotation Nous ne décrirons que les réactions observées à l arrêt d une rotation de sens horaire Il suffira, pour connaître les réactions de l animal à l arrêt d une rotation de sens antihoraire de remplacer le mot « droite » par le mot « gauche)

Vitesse 120 /s. La grenouille s incurve fortement vers la droite et effectue dans ce sens, un mouvement de manège continu ou seulement quelques déplacements (Fig 3 a)

60 /s L animal s incurve généralement fortement vers la droite incurvation qui peut se poursuivre par un ou plusieurs sauts (Fig 3 a)

30 /s. Incurvation moyenne vers la droite (Fig 3 b)

15 /s. Incurvation faible vers la droite (Fig 3 c)

8 /s Incurvation très faible vers la droite (Fig 3 d)

Chez une grenouille aveugle dont l appareil vestibulaire est intact les réactions rotatoires ne varient pas lorsqu on étudie l animal à plusieurs jours d intervalle Leur amplitude ne change pas sensiblement d un animal à l autre (La Fig 3 e représente une grenouille non incurvée)

2) *Le lendemain de la section des 2 nerfs utriculaires*

a) Réactions à l inclinaison vers la droite et vers la gauche Les 30 grenouilles étudiées n ont plus aucune réaction compensatrice à l inclinaison du support. Elles se comportent comme une masse inerte Toutefois, lorsque l inclinaison atteint une valeur importante (40 ou 50 environ) l animal glisse et réagit généralement en étendant le bras situé du côté le plus bas du plan incliné La grenouille adopte parfois une attitude compensatrice faible et fugace car le plus souvent elle perd son équilibre précaire et tombe Cette légère réaction compensatrice qui se produit lors d un glissement de l animal mais aussi lors d un mouvement de celui-ci est vraisemblablement due aux canaux *semi-circulaires verticaux*

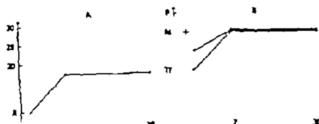


FIG. 5. (Même légende que 1 Fig 4) Les Figs 5 A et 5 B correspondent à la même grenouille. Sa f un, tous les animaux du groupe II donnent des graphiques semblables.

leur amplitude ne retrouve jamais une valeur normale On note même sur la courbe un palier qui débute une semaine ou un mois après l opération dans le cas de la grenouille représentée sur la Fig 4 l'incurvation, qui est faible à l arrêt d une rotation de 60 /s. une semaine après l opération, est toujours faible 1 mois, 2 mois et même 3 mois après la section des 2 nerfs utriculaires (Fig 4 B)

Groupe II 9 grenouilles

a) *Réactions à l'inclinaison vers la droite et vers la gauche* Les réactions compensatrices ont une amplitude de plus en plus importante à mesure que les semaines s écoulent, mais cette amplitude n atteint jamais une valeur normale (Fig. 5 A)

b) *Réactions à l'arrêt d'une rotation* L amplitude de l'incurvation est de plus en plu grande à mesure que s écoule le temps postopératoire 1 grenouille retr uve des réactions normales pour toutes les vitesses de rotation les autres conservent des réactions affaiblies (incurvation seulement faible ou moyenne à 120 /s. au lieu d une incurvatio n forte suivie de déplace ment (Fig 5 B))

Groupe III 8 grenouilles

a) *Réaction à l'inclinaison vers la droite et vers la gauche* L amplitude des réactions compensatrices redevient sensiblement normale au bout de plu ieurs semaines (Fig. 6 A)

b *Réactions a l'arrêt d'une rot tion* Les réactions postrotatoires retrouvent petit à petit un amplitude de plus en plu grande dont la valeur au b ut d plu ieurs semaines, est égale ou sensiblement égale à celle que l'on obser avant l opération (Fig. 6 B)

DISCUSSION ET CONCLUSION

La technique opératoire que nou avon utilisée pour la section du nerf utri ul ire permet de couper les fibres nerveuses sans les voir m is on risque de léser des fibres de la br nch antérieure du nerf vestibulaire et,

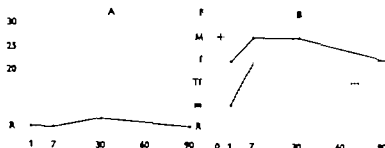


FIG. 4 (A) Réaction compensatrices à l'inclinaison. *En abscisses* j urs comptés à partir du j ur de l opération *en ordonnées* : valeur de l'inclinaison en degrés *R* aucune réacti n.

(B) Ré ctions rotatoires. *En abscisses* : jours comptés à partir du jour de l opération O grenouille aveugle dont l appareil vestibulaire est intact; *en ordonnées* amplitude d la réaction *R* aucune réaction *m* faible mou ment de tête *Tf* incurvation très faible *f* faibl *M* moyenn *F* forte a ec n sans déplacem nts. × amplitude des réactions postrotatoires des *grenouilles seulement aveugles pour les vitesses* d 120 et 60 /s + amplitud des réacti ns postrotatoires des grenouill s seulement veugles pour la vitesse de 30 /s. Trait plein: 120 / tirets: 60 /s. pointillés: 30 /s. Les Fig. 4 A et 4 B correspond nt à la même grenouille T us les animaux du groupe I donnent des graphiques semblables

15 /s 5 grenouilles s incurvent très faiblement vers la droite 23 animaux n effectuent qu un très faible mouvement de tête vers la droite ou bien ne présentent même aucune réaction

8 /s 15 animaux effectuent un faible mouvement de tête vers la droite mouvement qui n affecte nullement la symétrie de la grenouille 13 grenouilles n ont aucune réaction

3) Pour poursuivre l étude des réactions compensatrices et rotatoires et noter leur évolution dans le temps, nous distinguerons plusieurs groupes de grenouilles celles dont les réactions à l inclinaison restent nulles plusieurs *semaines après la section des 2 nerfs utriculaires (groupe I) celles* dont les réactions compensatrices réapparaissent petit à petit mais en *conservant une amplitude faible (groupe II) enfin celles dont les réactions* à l inclinaison retrouvent une amplitude sensiblement normale un certain nombre de semaines après l opération (groupe III) (Deux, des 28 grenouilles dont les réactions rotatoires avaient été modifiées par la section des nerfs utriculaires sont mortes après quelques jours et ne figurent par conséquent dans aucun des groupes I II et III)

Groupe I 9 grenouilles

a) Réactions à l inclinaison vers la droite et vers la gauche Les animaux ne présentent aucune réaction compensatrice même plusieurs semaines après l opération (Fig 4 A)

b) Réactions à l'arrêt d'une rotation Pour une même grenouille les réactions plusieurs semaines après la section des nerfs utriculaires, sont généralement un peu plus importantes qu au lendemain de l opération mais

tions compensatrices restent nulles au contraire, les réactions rotatoires retrouvent petit à petit une amplitude normale à mesure que les réactions compensatrices retrouvent, elles aussi une valeur plus élevée Si les nerfs des canaux horizontaux avaient été lésés il semblerait inexplicable que les fibres aient toujours régénéré chez certains animaux (ceux précisément chez lesquels les réactions compensatrices redeviennent normales) et pas chez les autres (ceux précisément chez lesquel les réactions compensatrices restent nulles)

b) Au lendemain de l'opération les animaux sautent ou marchent en ligne droite ou irrégulière mais sans tourner préférentiellement d un côté on ne note aucun mouvement de manège Dans l'eau d un aquarium, les grenouilles progressent également en ligne droite et ne présentent aucune tendance à tourner vers la droite ou vers la gauche Or on sait que la plus petite lésion du nerf d un canal horizontal se traduit sur le comportement de l animal qui effectue des mouvements de manège du côté lésé.

c) Enfin les réactions postrotatoires dirigées vers la droite et vers la gauche ont une amplitude égale Si des fibres des nerfs des canaux horizontaux avaient été lésées, il est hautement improbable que la lésion ait été identique des deux côtés.

D autre part des dissections et l étude de coupes histologiques[1] nous ont permis de vérifier l état des nerfs utriculaires et ampullaires ainsi que des m cules et des crêtes plusieurs semaines ou plusieurs mois après l'opération.

Chez 3 animaux du groupe I nous av ns effectué des coupes et av ns constaté que la macule utriculaire était dégénérée ou en voie de dégénérescence (Fig. 7) La dissection chez 3 animaux du groupe II n us a permis de constater que le nerf utriculaire avait régénéré en entier ou en partie l étude des coupe faite chez 2 autres grenouilles, nous a montré une image normale d la macule utriculaire (Fig 8) Enfin chez 6 animaux du groupe III nou avon vérifié par di section que les 2 nerfs utriculaires avaient régénéré

La réapparition des réaction compensatrices semble donc *être due* à une régénération du nerf de l'utricule d nt les fibres *réinnervent la m cule* utricul ire Parall l ment à la régén ration des fibres utriculaires et au retour progressif des ré tions compen atrices, nous avon *noté chez les* grenouilles, une position de repo qui redevenait normale *un réflexe de* retournement très rapide et un disparition des tremblement apr s un mouvement pontané

l observation des coupes n u a m ntré que la *crête ampullaire* des 2 canaux horiz ntaux et les nerf qui l'innervent étaient *n bon état*, l'image t nt identique à cell observée chez une grenouille *normale (Fig 9)* *Cette cr t* ampullaire est intact hez le grenouilles dont les réactions r tatoires sont redevenues n rmales, mais us i chez celles dont les réacti n rotatoi

[1] L'ect hon des oreilles été f it suiv t la tech ique d' ncl ion ml t collodion p raffine Les oupes, d'une épai seur d 10 ont été olorées à l'hémal ox line

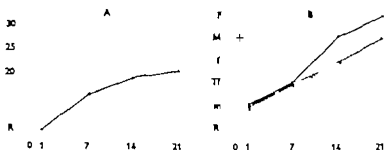


FIG. 6 (Même légende que la Fig. 4) Les Figs. 6 A et 6 B correspondent à la même grenouille Tous les animaux du groupe III d nent des graphiques semblables.

par conséquent des fibres du nerf ampullaire du canal horizontal Deux questions se posent alors

1 le nerf utriculaire a t il bien été coupé?

2° le nerf du canal horizontal n a t il pas été lésé?

Des observations précises portant sur le comportement des animaux nous permettront de répondre à ces 2 questions

1) Le nerf utriculaire a bien été coupé

a) Aucun des animaux étudiés ne prenait plus, au lendemain de l opération *de position compensatrice a l inclinaison du support* quel que soit le sens de cette inclinaison

b) L attitude de repos d une grenouille opérée et d une grenouille aveugle dont l appareil vestibulaire est intact est différente La première a le dos *horizontal et la tête légerement fléchie alors que* le dos de la seconde est plus ou moins oblique et le museau horizontal Les grenouilles opérées conservent toujours une attitude symétrique ce qui ne serait pas le cas si les deux nerfs utriculaires avaient été coupés de façon incomplète et, dans *ce cas, l attitude serait presque à coup sûr non exactement symétrique*

c) Placée sur le dos, la grenouille privée des 2 utricules se retourne indifféremment du côté droit ou gauche mais ce réflexe est beaucoup moins rapide qu avant l opération

d) La grenouille opérée se déplace spontanément mais saute rarement (dans ce cas les sauts sont courts) Elle marche ou rampe le plus souvent le museau fléchi touchant parfois le sol Après un mouvement spontané la majorité des grenouilles opérées présente des tremblements caractéristiques d amplitude plus ou moins grande qui durent 1 ou 2 secondes Ces observations sont en accord avec celles de Tait & McNally (1934)

2) *Les nerfs des canaux semi-circulaires hori ontaux n ont pas été lésés*

a) Nous avons *remarqué en exposant les résultats,* qu il *existait* un parallélisme étroit entre les reactions à l inclinaison du support et les réactions rotatoires dans le plan horizontal (comparer les Figs. 4 A et 4 B 5 A et 5 B 6 A et 6 B) ces dernières restent de faible amplitude si les réac

tions compensatrices restent nulles au contraire, les réactions rotatoires retrouvent petit à petit une amplitude normale à mesure que les réactions compensatrices retrouvent, elles aussi une valeur plus élevée Si les nerfs des canaux horizontaux avaient été lésés il semblerait inexplicable que les fibres aient toujours régénéré chez certains animaux (ceux précisément chez lesquels les réactions compensatrices redeviennent normales) et pas chez les autres (ceux préci ément chez lesquels les réactions compensatrices restent nulles)

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c) Enfin, les réactions postrotatoires dirigées vers la droite et vers la gauche ont une amplitude égale Si des fibres des nerfs des canaux horizontaux avaient été lésées, il est hautement improbable que la lésion ait été identique des deux côtés.

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La réapparition des réactions compensatrices semble donc être due à une régénération du nerf de l utricule dont les fibres réinn rvent la macule *utriculaire Parallèlement à la régénération des fibres utriculaires* et au retour progressif des réacti ns compensatrices, nous avons noté, chez les grenouilles, une position de repos qui redevenait normale un réflexe de ret urnement très rapide et une di parition des tremblements après un mou ement pontané

L bservation des coupes nous a montré que la crête ampullaire des 2 canaux horizontaux et les nerf qui l'innervent étaient en bon état, l'image étant identique à celle observée chez une grenouille normale (Fig. 9) Cette crête mpullaire est intacte chez les grenouilles dont les réaction rotatoires sont redevenues normales, mais aus i chez celles dont les réaction r tatoi

L'inclusion des oreilles été fait vant la tech iqu d'inclu l mixte collodion-paraffine Les coupes, d'une épaisseur de 10 μ, ont été colorées à l'hém lun-éosine

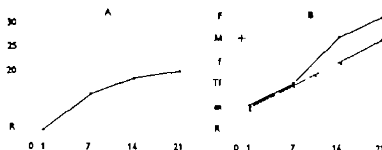


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par conséquent des fibres du nerf ampullaire du canal horizontal Deux questions se posent alors

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2° le nerf du canal horizontal n a t il pas été lésé?

Des observations précises portant sur le comportement des animaux nous permettront de répondre à ces 2 questions

1) Le nerf utriculaire a bien été coupé

a) Aucun des animaux étudiés ne prenait plus, au lendemain de l opéra tion de position compensatrice à l inclinaison du support quel que soit le sens de cette inclinaison

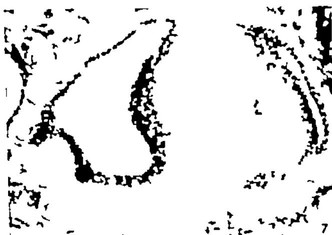
b) L attitude de repos d une grenouille opérée et d une grenouille aveugle dont l appareil vestibulaire est intact est différente La première a le dos horizontal et la tête légèrement fléchie alors que le dos de la seconde est plus ou moins oblique et le museau horizontal Les grenouilles opérées conservent toujours une attitude symétrique ce qui ne serait pas le cas si les deux nerfs utriculaires avaient été coupes de façon incomplète et, dans ce cas l attitude serait presque à coup sûr non exactement symétrique

c) Placée sur le dos, la grenouille privée des 2 utricules se retourne in différemment du côté droit ou gauche, mais ce réflexe est beaucoup moins rapide qu avant l opération

d) La grenouille opérée se déplace spontanément mais saute rarement (dans ce cas les sauts sont courts) Elle marche ou rampe le plus souvent le museau fléchi touchant parfois le sol Après un mouvement spontané la majorité des grenouilles opérées présente des tremblements caractéristiques d amplitude plus ou moins grande qui durent 1 ou 2 secondes Ces obser vations sont en accord avec celles de Tait & McNally (1934)

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a) Nous avons remarqué en exposant les résultats qu il existait un parallélisme étroit entre les reactions à l inclinaison du support et les réac tions rotatoires dans le plan horizontal (comparer les Figs 4 A et 4 B 5 A et 5 B 6 A et 6 B) ces derni res restent de faible amplitude si les réac


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8


9

res sont restées faibles et dont la macule utriculaire a dégénéré. Or on sait que la section d un nerf ampullaire entraîne la dégénérescence de la crête (Gribenski 1963) Toutes ces observations montrent que la perte plus ou moins importante des réactions rotatoires n est pas due à une lésion des *nerfs ampullaires des canaux horizontaux mais bien à l élimination fonctionnelle des 2 utricules*

En conclusion on peut dire que l élimination fonctionnelle des 2 utricules par section des nerfs utriculaires provoque, chez la Grenouille, une diminution plus ou moins importante de l amplitude des réactions postrotatoires dues à la stimulation des canaux semi-circulaires horizontaux

Nous essaierons dans un prochain travail de savoir *quelle est la nature* des relations qui existent entre les appareils utriculaire et ampullaire.

SUMMARY

We have studied the vestibular postrotatory reactions (reactions elicited by the stimulation of the horizontal semi-circular canals) in the frog, blinded by section of optic nerves before and after section of the utricular nerves. For each rotation speed the reaction at the stopping of the rotation is smaller when the utricular nerves have been cut on both sides. Yet, the horizontal semi-circular canals and their ampullar nerves are undamaged and the cristae according to histological examination are normal We may conclude that the reactions elicited by the stimulation of the horizontal canals are smaller in the animal without utricules than with utricules (this difference has not the same value for every frog)

ZUSAMMENFASSUNG

Es wurden die postrotatorischen Vestibularreaktionen Reaktionen die durch die Reizung der semizirkulären horizontalen Kanäle hervorgerufen werden am Frosch studiert der durch einen Schnitt der optischen Nerven erblindet ist. Man beobachtete diese Reaktionen vor und nach dem Schnitt durch den Nervus utricularis. Für ein und dieselbe Rotationsgeschwindigkeit sind die beobachteten Reaktionen am Ende der Rotationsbewegung schwächer bei einem Frosch, dem beide Nervi utriculari durchtrennt wurden als bei einem Frosch der nur die Sehfähigkeit verloren hat Die semizirkulären horizontalen Kanäle jedoch ebenso wie die Nervi ampullari sind intakt Die Cristae erscheinen bei einer histologischen Untersuchung normal. Daraus wird geschlossen dass der Verlust des Utriculus

FIG. 7 Macul utriculaire 3 semai es près la secti du nerf utriculaire La macul est en ole de dégénérescence (coupe ho izont l)

FIG. 8. Macule utri ulaire, 2 mois après la secti n du nerf utriculaire Les fibres ne veuses ont régénéré t la macul a u structure n rmal (co pe h rizont l)

FIG. 9 Crête ampullaire d un c nal horizontal, 2 moi et d mi près la section des 2 nerfs utriculaires. La crêt a une tructure normal (coupe horiz tal)

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COCHLEAR DEVELOPMENT

Some Electron Microscopic Observations of Maturation of Hair Cells Spiral Ganglion and Reissner's Membrane

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Th hai cells differentiat before their erve endings m ke synapti co tact in th rgan of Corti. Each hair cell develops stereocilia d a cuticle prior to in ervation The ectoderm l end lymph tic layer of R issner' m mbran has some fe tures in common with fluid tra sport epithelia. Each piral ganglion Schwann cell initially envelop many erv fibers, but vent lly my linates only si gle fiber

Do cochlear hair cells begin to differentiate and develop recognizable char acteristics befor they are innervated We have been unable to answer this questi n from the li] rature Friedmann (1959) studied early events in chick otocyst tis ue culture by electron microscopy and Ruben (1967) has used tritiated thymidine to label terminal mitoses in the cochlea In rabbits, different ~ begin at about the 22nd day of life. This stage is reached by humans at the 62 mm or twelve week stage (Bast & Anson, 1949) Our group has previously discussed some event which occur during l ter stages f maturati n of the organ of Corti (Kikuchi & Hilding, 1965) and stria vasculari in mice (Kiku hi & Hilding, 1966) and in mink (Hil ding t al 1967) Bast & Anson (1949) explained the main events of coch lear dev l pment R tziu (1884) depicted most developmental features t the rgan f Corti with excellent accuracy Cimino & Grisanti (1967) recently published a light microscopic tudy of cochlear de el pment

Reissner membran separ tes th perilymph of scala media and endolymph f th cochlear duct Ch u (1963) showed that it is very active metabolically and several experiment (Lawrence et al 1961 Rauch et al 1963) uggest th t it employs active transport to aid in producing ionic d fferences. It contain oxidative enzymes, (N mura & Balogh 1964 Nakai & H lding, 1968) nd ATP-ase i present in its endolymphatic layer of cells (Nak i & Hilding, 1967) Recently Duvall (1967) and Iurato (1967) ha e described it lectron microscopi structure. The nature f Reissner mem

Thi tudy pported by Public Health Service Research Grant from the N tional Institut of Neurological Diseases nd Blindness (NB 03993 nd NB 07159) and grant from the Deafness Research Foundation

die Reaktionen vermindert die durch die Anregung der semizirkulären horizontalen Gefässe hervorgerufen werden Diese Abschwächung ist mehr oder weniger wichtig bei den verschiedenen Lebewesen und *bei einigen gar nicht vorhanden*

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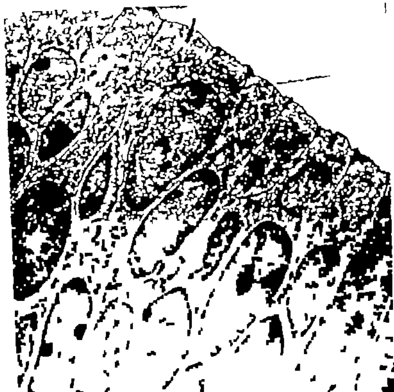
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Labo toi e de Biolog e im l
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brane has been of interest because of the large difference between endolymph and perilymph in chemical content (Smith *et al.*, 1954) and electrical potential (Békésy 1952)

The cell bodies of the neurons of the spiral ganglion are unique because they are covered with several Schwann cell layers.

Rosenbluth (1962) has described in detail several different patterns of myelination that can be distinguished with electron microscopy in the adult spiral ganglion

The purpose of this paper is to present electron microscopic findings in fetal rabbits during some early stages of differentiation of the organ of Corti to discuss some observations on Reissner's membrane and to describe some patterns of early myelin formation

MATERIALS AND METHODS

Rabbit fetuses were obtained by Caesarian section at stages varying from 22 to 30 days after mating Specimens from newborn and adult mice were used for comparison

As quickly after death as possible the temporal bones were removed and openings made through the bony wall of the cochlea to permit access of fixative solutions The modiolus was opened in some animals to permit fixation of the spiral ganglion We used either 1% osmium tetroxide buffered with 0 1 M phosphate or 3% glutaraldehyde in 0 1 M cacodylate buffer followed by osmium textroxide After dehydration they were imbedded in Epon After the plastic had hardened a fine saw was used to divide the

FIG. 1 Orga of Corti, pical tu n of 22-d rabbit f t Thi f ture nsory epith lium n i t f pseudost tified column cell Th re n rec gnizabl charact ristics that would d ntify fut re h i o upp rting cell N m ro illi stereocilia ha ppeared, but k noc il re f und t th d l mphati surf ce 7500

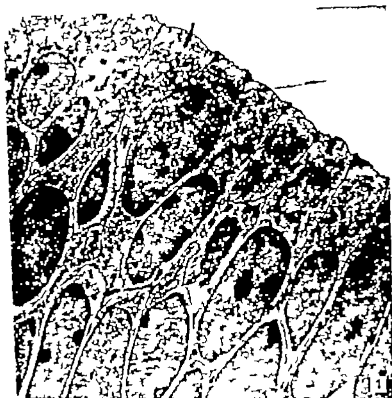
FIG. 2. High m gnificati f the sam 22-day pical turn rg f Corti, howing ki ocilium (*K*) nd it rootl t (*R*) Th upper d f h f h cell i urro ded b j n ti l mpl res mbli g ula adh ren (*ZA*) wh h w ll l ter become part f th reti ul plat 42,000

FIG. 3 Org f Corti iddl turn, 22-da fetus. The middl turn i lightl m re d need tha th api l, d future h i cell can be id t i d b it cutic l (*C*) nd de l p g t reocilia N ghbo i g upport ng cell ha mall mi ro illi 10,000

FIG. 4 Sam m ddl turn, org f Corti, t 22 d h w i g n fibers pa i g betwee hair cll (*H*(d upporti g cells. At th i st g w f u d t pical n pses, d only this uggest f l napse f rm ti (S 15,000

FIG. 5 High m g ti middl turn, 22-d org f Cort sh w g ppe porti of future hai cell Th soll t (*a* *m*) d f bril of th ki ocili m re i ibl Th tereocilia (*S*) h begu t devel p, but thei rootlet h not ppe red lthough th cuticl (*C*) has. 85,000

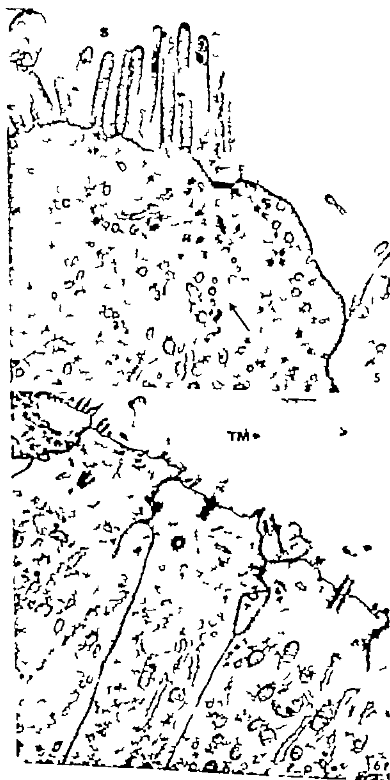
FIG. 6 Lowe turn, 22 da s, r f ture i r leu Th tectorial membrane (*TM*) h begun t ppear 30,000


1


ZA
K
R
2


C
3


HC
4


S
TC
5
TM
6

cochlea into several blocks which were remounted for sectioning Free hand sections were made for phase contrast light microscopy and an LKB Ultrotome was used for making sections for study with an RCA EMU 3G electron *microscope The sections were stained with saturated uranyl* acetate in 50% ethanol

FINDINGS

Different stages of maturation could be studied in the same specimen because development tends to proceed from the basal turn towards the apex and each specimen showed a spectrum of varying maturity

The least developed area that we studied was the apical turn of the rabbit fetus at 22 days (Fig 1) The future organ of Corti consisted of two or three layers of pseudostratified columnar cells resting on a basement membrane The hair cells could not be distinguished from those that were destined to become supporting cells At the top of each cell was a pair of *centrioles, one of them having a kinocilium No microvilli were seen and* the tectorial membrane was not present Neither nerve fibers nor endings were identified

Lower turns of the same 22-day cochleas showed several more advanced features (Figs 3–8) Hair cells had differentiated enough to permit their identification and nerve fibers were found between cells Although it was difficult to be sure that no synaptic areas had formed and an occasional spot suggesting early synapse formation was seen, most hair cells seemed to have become differentiated without evidence of typical synapse formation They had club-shaped stereocilia that were longer and thicker than the microvilli of neighboring supporting cells. At the apical end of each

FIG 7 Spi l ga gli 22-d y f tus. The Schw n (S) cell t l da ker tha d the neuron (N) F ntu lly ea h n uron will be myeli ted but t thi rly at ge nl f w thin Schw nn cell proce se h v begun to separat th neurons. 7500

F G 8 D nd ltes f piral g ngl n lls, 22 days. M t fibers re still unco ered, but n l pm t by Schw nn cell h begun 7500

F G 9 Spiral g nglion, 27-day f tus. The euro cell bodi are m re complet l covered Separat processes from a i gl Schw n cell som times wrap cell bod nd dj cent ers f bers 15,000

FIG. 10 Tw nty se n da s. N rv fibers re m re complet ly wrapped b thi tage 15,000

FIG. 11 Org f Co ti, l y pse form ti n, 27-d rg of Corti basal turn Syn pti bars a d cell m mbran thick ning fulfill th morpoh l gical critera f r ffer ent y pses Som n *ndi gs penet t l to the cell* t thi st g lmit ti g the appe rance f the primiti se sory pithell m of th l t ral line rg ad it fl h. 42,000

FIG. 12. Basal turn, n wborn rg n f Corti f the m use N rv di gs t base f out r hai cell Alth ugh th b l cell ha n in gination (*I*) n a ers ndi g the afferent ndi gs re clust red utsid th hai cell 120,000


N
N
N
7


8

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F Spiral gangli n, 22-d y f tus. Th Schwann (S) cell st in d rke tha d th n u n (N) E tuall ea h n uro will be my l n ted b t at thi ea ly t ge) a few thin Schwann cell proces hav begun t separat the neurons. 300

Fig 8 Dend it s f piral g nglion cells, 22 da s. M t fibers re still u co ered, b t n l pm t by Sel wan cells ha beg n. 7300

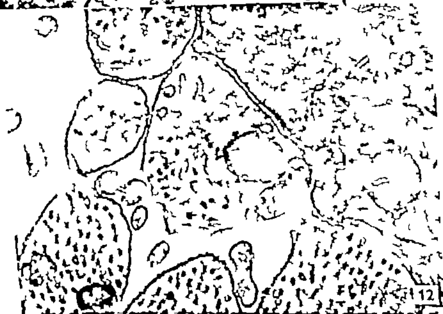
Fi 9 Spiral g ngli n, 27-d y fetus. Th n uro cell bod es re more complet l co ered Separat proce es from s gl Schwan cell somet mes wr p cell bod d djacent nerv fibers 15 000

F a 10 Tw nt e days. N rv fibers are m re complet l wrapped b thi l g 15,000

Fig 11 Organ of Co ti, l synapse f rmat 27-day rgan of Corti basal turn S n ptl bars nd cell membran thick n g fulf ll th morpoh logical crit ra for affer nt sy apses Som erv ndi g penetrat l t the ll t thi st ge imitati g the appe rance f the m re primiti se ry pitheli m f th l teral line orga l adult fish. 42,000

F a 12 Basal turn, newborn rg n f Corti of the m use N rv endi g t base f out r hair cell Although the hai cell ha in gl ti n (I) ea nerv nding, these afferent dings are in tered ut d the h i cell 120 000

11




9


10


13


14

hair cell was a homogeneous zone beneath the stereocilia that was very similar to the cuticle of adult hair cells The rootlets that form the core of adult stereocilia and pass into the cuticle were not seen at this stage The tectorial membrane was identified (Fig 6)

Neurons and Schwann cells can be identified in the spiral ganglion of the middle turn of the 22-day fetus as illustrated in Fig 7 The Schwann cells have dark cytoplasm that forms long thin processes that have begun to wrap around nerve cell bodies and between bundles of nerve fibers as seen in Fig 8 By the 27-day stage the pattern of envelopment by Schwann cell processes showed progression Multiple layers of Schwann cell cytoplasm surrounds the cell bodies (Fig 9) and Schwann cell processes have become insinuated between nerve fibers

There were abundant nerve endings in the 27-day stage By their paucity of synaptic vesicles and because "synaptic bars" were often found opposite within the hair cell (Fig 11) they were classified as afferent endings An interesting feature of this stage is the position of some nerve endings with respect to the hair cells Like the pattern of the lateral line organ as described by Flock (1965) some of these endings penetrate into the hair cell cytoplasm A few were almost completely enveloped by the hair cell as seen in Fig 11 As maturation proceeds, the hair cells and nerve endings come to occupy the relation illustrated in Fig 12 forming a cluster at the rounded base of the hair cell The transitional stage of hair cell invagination by nerve endings mimicking the more primitive lateral line organ seems to be another example of mammalian ontogeny following a phylogenetic precedent

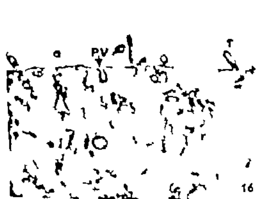
At the newborn stage nerve fibers of the spiral ganglion were surrounded by a rather heavy layer of Schwann cell cytoplasm but wrapping of multiple layers was not evident (Fig 13) (Newborn mouse specimens were used for these illustrations because of fixation difficulties with our newborn rabbits) In the basal turn some fibers are covered by several layers as seen in Fig 14 We have been unable to find examples of a single Schwann cell wrapping multiple layers around more than a single nerve fiber or cell body and have been at a loss to understand the process whereby the pattern of multiple fiber envelopment as illustrated in Fig 13 is replaced by one-to-one relationship of Fig 14

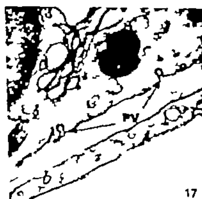
Figure 15 illustrates the simple cuboidal form of the cells of the endo-

Fig 13. Nerve fibre with the piral g gli n, n wborn middle t rn N l rs fibe ha been wrapped. Tw Schw cell (S) f rm rs complicated pattern th y cover the fibers f th bu dl Fibrobl t (F) ha less d se cyt pl m nd basement membran (M m) 15,000

Fig. 14 Newborn piral g gl n, ly m ll sheath formati n m ltipl l ers wrap fiber (F) There is ha y l y o the uter urface f th Schwa cell rs fiber complex that represent l basem t m mbra (BM) formation (M se) 60 000

15









lymphatic layer of Reissner's membrane at the time of birth in mice. Some interdigitation between cells was found but few microvilli or pinocytotic vesicles. Each endolymphatic layer cell like all the others lining scala media at this stage had a single kinocilium. Multiple layers of perilymphatic cells are reduced to a single layer as development proceeds.

Several features were evident in Reissner's membrane from adult specimens that are relevant to its possible role in transport. Microvilli cover its endolymphatic surface, increasing the surface area of these cells (Fig. 16). Pinocytotic vesicles were found on both inner and outer surfaces of both the endolymphatic layer of cells (Figs. 16, 17 and 19). Karnovsky (1967) has recently studied ultrastructural and cytochemical features of the junctions between cells and stressed the importance of these to transport phenomena, particularly to the concept of "holes" as required by Pappenheimer's transport theory (1953). Figure 18 illustrates the types of junctions that can be demonstrated in Reissner's membrane.

Figure 21 shows the commonest myelin pattern that we found around the cell bodies of adult spiral ganglion cells. About twelve layers of rather light staining myelin are found with a fairly thick Schwann cell cytoplasm layer on the inner and outer side. A basement membrane is the outermost layer. Some neuron cell bodies had more compact myelination and others were wrapped by only a few layers of fairly thick cytoplasm. These results confirm Rosenbluth's observations (1962).

DISCUSSION

Pinocytotic vesicles are present on each side of both layers of the adult Reissner's membrane. Although Marchesi's & Barrnett's (1963) electron microscopic histochemical study demonstrated ATP ase an enzyme associ

Fig. 1 R i m bra wborn m use. These cell re o th d l mphatic d f R i membran Th re cubold l, with som i terd g tati between cell d t ba m t m mb Th k oc lium w ll d ppe th cochlea com pl tes it n to tl t n g f two three weeks.

Figs. 16 19 R i sner' m mbran dult m se. Th re re tw cell l yers the matur m mbra sepa ted by basem t m ml n d m eo nect tl e. These f gures illu trat m f tu es that may be of ig ifl nce to t n port ph m na ro the m mbra

Fig. 16 Pinoc tot cal l (PV) nd mi ro illi the rf ce f th d l mphati layer f cing nd l mph

Fig. 17 Pinocyt ti l les (PV) basem t m mbran d f d l mphatic l er

Fig. 18 J ncti l compl betwee nd lymphati l ye cells. Z l occlud (ZO) Zonula adhere s (ZA) nd M cul dhera (MA) W did n t obt in enough resol tion t determin wh th r or n t m ll pa sag wa l t betwee cell t th zo la occludens.

Fig. 19 Pinocytotic icles (PV) n both rface of perilymph tic layer cell


20
21

ated with active transport in relation to these vesicles, it is not yet certain what role they may serve in electrolytic transport. As illustrated in Figs. 16, 17 and 19 open mouthed vesicles are present on the endolymphatic layer and on each surface of the perilymphatic cell layer. We have been unable to find any similar example of four layers of pinocytotic vesicles in a single structure. It seems likely that substances are being transported by this means in one or both directions across Reissner's membrane.

A recent paper on gallbladder epithelium suggested that fluid passes in the space between interdigitating cell processes and that its composition is altered as it flows over the very large cell surface to which it is exposed (Kaye *et al.* 1966). It was shown that the dimensions of this space change remarkably in different physiological situations. Similar variations in this type of space between cells with folded processes occur in the endolymph secreting epithelium of the frog according to unpublished work by E. Simon from our laboratory. The fact that ATPase is present on the opposed membranes of this space is additional evidence that active transport occurs. To drive its 'pumps' Reissner's membrane must obtain energy from surrounding fluids since it has no vasculature of its own. According to pipette studies, oxygen is higher in endolymph (Misrahy *et al.* 1958). Perhaps this explains why only the endolymphatic layer of Reissner's contains ATPase.

As discussed in earlier electron microscopic reports, the microvilli of Reissner's membrane are another means of facilitating the passage of fluid by increase of surface area (Lawrence *et al.* 1961, Friedmann 1959). Rauch *et al.* (1963) reported that potassium passed quickly into endolymph. From these results and from its morphology one might guess that Reissner's membrane actively transports sodium away from endolymph and facilitates the transfer of potassium into endolymph.

Politzer (1956) presented evidence that the spiral ganglion is derived from the otocyst and not from the neural crest. Streeter (1906) was an early advocate of this concept. In 1962, Rosenbluth showed that eighth nerve cell bodies are wrapped by a sheath of myelin. Electron microscopists have not reported any other kind of myelinated nerve cell body. We have no evidence from this study with regard to the question of origin of spiral ganglion cells, however it is interesting to speculate if their unique myelin pattern may also be related to their unusual developmental heritage. Are spiral ganglion Schwann cells also of otocyst derivation?

Differentiation of hair cells begins before they are innervated or at least before they make synaptic contact with their nerve endings. One can recognize the hair cells by their cuticle and stereocilia in the mid and lower

Fig. 20. Newborn mouse spiral ganglion basal turn. M... approaching completion ... fiber is wrapped with two ... 120 000

Fig. 21. Adult mouse spiral ganglion. Several layers of myelin around this neuron cell body (N) and an adjacent myelinated fiber illustrates the normal dense pattern of myelination.


20
N
21

turns of the 22-day stage At this stage nerve fibers can be demonstrated winding their way between the cells of the future organ of Corti, but no typical nerve endings were found We have been unable to discover whether analogous sensory organs similarly begin differentiation prior to innervation In the retina ganglion cells undergo terminal mitosis before the photoreceptor cells Lasansky & de Robertis (1960) described synaptic vesicle accumulation in visual cells before synapses formed Taste buds can be grown in transplanted oral mucous membrane which lack normal innervation (Stone 1940) but we have found no electron microscopic studies of early differentiation of taste bud cells

ZUSAMMENFASSUNG

Die Haarzellen können bevor ihre Nervenfasern Kontakt nehmen durch ihre Stereozilien und Kutikula identifiziert werden Die ektodermale endolymphatische Schicht der Reissnerschen Membran hat einige Eigenschaften mit Epithelien welche Flüssigkeit transportieren gemeinsam Jede Schwannsche Zelle des Spiralganglions umschliesst anfänglich mehrere Nervenfasern myelinisiert schliesslich jedoch nur eine Nervenfaser

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SOME SURFACE VIEWS OF THE STRIA VASCULARIS AND ITS ADJACENT AREAS

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The surface views of the stria vascularis and its adjacent areas are presented after a silver reaction a glutamic dehydrogenase staining and a H 3-uridine autoradiography Between the stria vascularis and the spiral prominence as well as Reissner's membrane some rows of spindle-formed cells were observed on the endolymphatic surface running parallel to the stria vascularis from the base to the apex of the cochlea The H-3-uridine autoradiography of the endolymph administration revealed distinct labels of the stria vascularis and the spiral prominence From these results, the resorptive function of the stria vascularis and the spiral prominence is discussed

The structure of the stria vascularis has been subject to many examinations Light and electronmicroscopic examinations of the stria vascularis seem to be now complete with respect to its major outlines. A good historical review of this structure was made by Nachlas & Lurie (1951)

Electronmicroscopic studies made by Smith (1957) Engstrom *et al* (1955) Echandia & Burgos (1965) Rauch & Ruska (1965) and Nakayama (1968) provided us with many fine photographs of *cytological details.* In the light microscopic studies we can find a good description by v Fieandt & Saxén (1936) Recently Kikuchi & Hilding (1966) presented their embryological studies by electronmicroscopy and differentiated the epithelial cells from the mesenchymal cells within the stria vascularis itself

The purpose of this study is to show the surface view of the stria vascularis and its adjacent areas under a light microscope A light microscopic photograph of the surface area of the stria vascularis hitherto failed to reveal clear structural profiles because of some considerable thickness of the stria vascularis

In this study a silver reaction and a glutamic dehydrogenase staining using nitroblue tetrazolium were employed for the structural analysis and a H-3-uridine autoradiography was carried out with the dissected materials of the stria vascularis and the spiral prominence of the guinea pig s cochlea.

METHODS

Cochleas of the albino guinea pig cat, albino rabbit and dog were studied They were anesthetized with the intra peritoneal administration of sodium pentobarbital (30 mg/kg) After decapitation the temporal bones were re-

moved and the oval and round window were exposed through the bulla. At the apex of the cochlea a small hole was chisled with rupture of Reissner's membrane by using a sharp needle. After extraction of the stapes the round window membrane was opened and a small hole was made through the basilar membrane of the first turn of the cochlea. A 0.2% AgNO solution at a temperature of 2–5 C was allowed to run through the cochlea with slight hydrostatic pressure in the same solution by using a small syringe. These materials were kept in a cold and dark chamber for 15 minutes, then the cochleas were washed with a 0.2% NaOH or a KOH solution for a few seconds and immersed in a 10% formalin in a cold and dark chamber for 24 hours. The bony capsule of the cochlea was chiseled away and the stria vascularis was dissected free in a suitable length sometimes with the spiral ligament attached.

Dehydrogenases can be demonstrated histochemically by using a tetrazolium salt (Pearse 1961). Nitroblue-tetrazolium is colorless, but it turns into a blue and insoluble formazan on reduction. For the demonstration of glutamic dehydrogenase activity in this study the following substrate solution was prepared

0.2% nitroblue tetrazolium	5 ml
0.25 M (pH 7.7) phosphate buffer	5 ml
0.05 M magnesium chloride	2 ml
0.2 M sodium glutamate	2 ml
DPN	10 mg
Ad. aq dest	16 ml

This substrate solution was allowed to run through the cochlea after the same operati e procedures as described above. The cochleas were incubated in this substrate solution for 30 minutes at 37 C. The *fixation* was done by using a 10% formalin solution for 24 hours. A careful *dissection* was carried out under a binocular dissecting microscope with magnifications from 5 to 20.

For the autoradiography H-3-uridine (1230 mc/mM The Radiochemical Center Amersham, England) wa used for the *intra-labyrinthine* administration into the end lymph of the guinea pig's cochlea. The *isotope* (*0.03* mc) was injected into the end lymph after boring a small hole at the basal and the third turn of the cochlea of the anesthetized *animal* by using a small glass capillary. Both holes were then packed with grease. Thirty m nutes after the injection the animal were *decapitated* and the cochleas were washed with running water and fixed in a 10% formalin added with 6 trichlor acetic acid for 24 hours. *The dipping* method (Joftes, 1959) was adopted for photographic procedures. The photographic exposure tim was 14 days. In another series of experiments, the same amount of H-3-uridine wa injected intraperit neally in order to rule out the labels through the blood circulation.

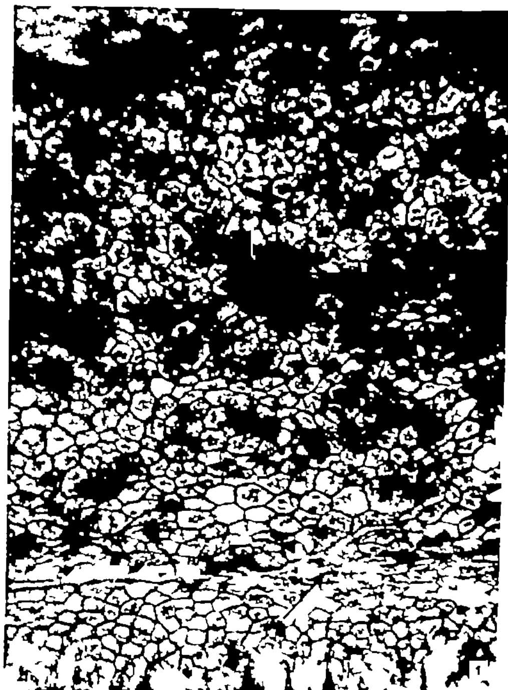


FIG. 1 Th t l sculari nd th p ral promin e i w d from th id f th scal media Betw the tria v scula l nd th piral promi nce pi dle-f rmed cell of l gitudinal rrang m nt (bord ri g cell) are l ibl (*a rowed*) R bbit cochlea Middl turn Sil e reacti n

RESULTS

With regard to the components of the stria vascularis, four different kinds of cells are known (1) a single layer of marginal (dark) cells which face the endolymph (2) intermediate (light) cells which locate beneath the marginal cells (3) a basal cell layer of two or three cell thickness which

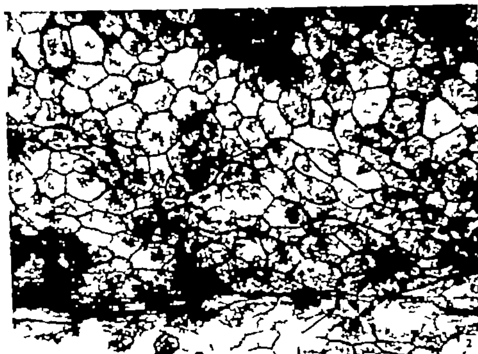


Fig 2. The high-power iew of the bordering cell bet ee the stri scularis and the spiral prominence (arrowed) Rabbit cochlea. Sil er reaction.

connects the stria asculari to the spiral ligament and (4) endothelial cells of the capillary netw rk of the stria vascularis which locates in the epithelium

The free surface of the stria vascularis is covered only with the marginal cells. It is a columnar type of cell with a smooth free surface bearing in some cases sparse short mier villi. According to Echandia & Burgos (1965) near the free surf ce the cells are firmly held together by zonulae occlu dentes and a few sm all desmosomes. Bel w the apical zone no desmosomes are bserved and the marginal cell become isolated from each other by interposition of ascending prolongations of the basal cells.

Figure 1 I an enti e width of the stria vascularis and the spiral prominence f the rabbit s cochlea viewed from the side of the scala media. The free surf ce of the marginal cell of the stria vascularis varies in size How ever n regi nal differences and n pecial cell arrangements were detect able The stria vascularis wa wider in the base nd it gradually narrows t ward th pex f the cochlea Between the stria vascularis and the spical prominence 2–3 rows of pindle-formed cell of considerable length were bserved (Figs. 1 and 2 rrowed) in all cochleas of the tested animals Morphologically these cell were very different from the marginal cells of th tria vascular and th epithelial cells of the spiral prominence They were running par llel t the tria vascularis and their nucleus was oval in

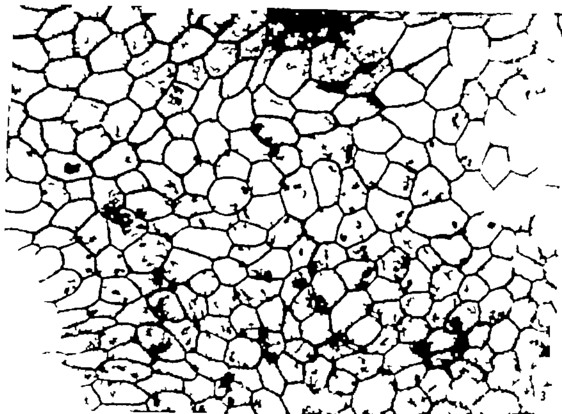


FIG 3 The marginal cell of th tria ascul ris viewed from the sid of the scala media Cat s coc lea Sil er reaction

shape and located in the center of the cell On the other hand the endolym phatic surface of the marginal cell and that of the spiral prominence cell was pentagonal or hexagonal in shape

Figure 3 is the surface view of the marginal cells of the stria vascularis of the cat s cochlea The contour of the free surface is clearly visible Most marginal cells were irregularly hexagonal in shape some were large and others small

The sectioned specimen showed that the nucleus of the marginal cell located close to the free surface Electronmicroscopy (Smith 195/ Naka yama, 1968) showed that the nucleus of the marginal cell of the stria vascularis of the guinea pig s cochlea was oval in shape with an indentation and usually displaced to one side of the cell Figure 4 is the surface view of the stria vascularis of the guinea pig's cochlea after a glutamic dehydro-genase staining The cytoplasm shows a dark coloration but the nucleus is not stained A potato-shaped nucleus (Nakayama 1968) with some inden tations in some cases, is conspicuous and the nucleus is obviously displaced to one side of the cell The functional significance of this eccentric location of the nucleus is still unknown At the upper limits of the stria vasculari (Fig 4 arrowed) one or two rows of spindle-formed cells were observable They interposed between the stria vascularis and Reissner s membrane and connected the marginal cell of the stria vascularis with the epithelial cell

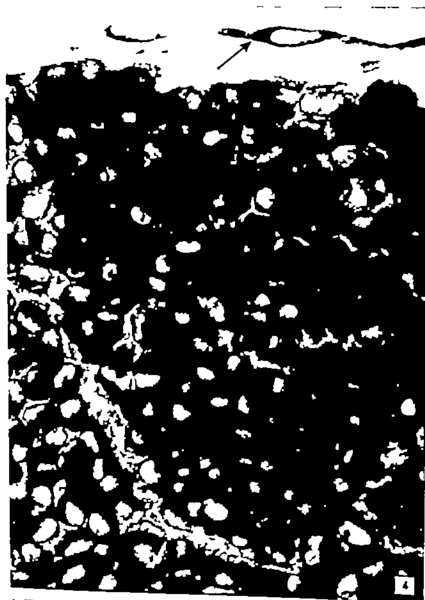


Fig. 4 The surface iew of the tria ascul ris after gl tamic dehydrog nase at 1 ing. Bet een the stri scularl nd R isner membrane, pl die-formed cell of longitu d nal rrangement bordering cells re sibl (rrowed) Guinea pig cochlea.

f R sner membrane These bordering cell were running parallel to the band f the stria vascul ri from the base to the apex of the cochlea.

Figure 1 the urf ce iew f th piral prominence and adjacent areas f the guinea pig' cochlea after il er reaction. The piral prominence is 3–6 cell wid in the guinea pig' cochlea and 10–12 cells wide in the rabbit s cochlea. Th free urface of each cell wa mostly hexagonal in shape but

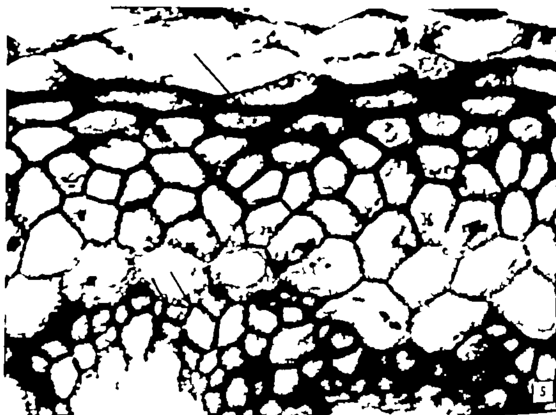


Fig. 5 The surface iew f th spiral promi nce and adjacent reas f the guinea pig's cochlea Between the stria vascul ri nd the piral prominence pindle-formed border ing cells re visibl (/) And between the spiral promi nce nd th external sulcus, an abrupt tran ition is present (//)

pentagonal in some cells According to Smith (1957) the spiral prominence is covered by one layer of osmiophilic cells which show microvilli on the endolymphatic surface These cells rest on a basement membrane which separates them from the spiral ligament below Adjacent cells are tightly joined as evidenced by terminal bars near the free surface The spiral prominence cells are arranged extending from the stria vascularis to the exter nal spiral sulcus, where there is an abrupt transition in cell structure This sudden transition is clear in Fig 5 The free surface cell of the exter nal spiral sulcus was very small as compared with that of the spiral prominence Figure 5 shows that the free surface of the spiral prominence cell is larger towards the external spiral sulcus, but this may be a prepara tion artifact

The autoradiograph of the stria vascularis of the guinea pig's cochlea revealed a distinct incorporation of H-3 uridine into the nuclear RNA after 30 minutes incubation with the isotope Figure 6 is a surface view of the lateral wall of the ductus cochlearis after removal of Reissner's membrane and the basilar membrane The marginal cells of the stria vascu laris and the epithelial cells of the spiral prominence showed massive silver grains on the nuclear region These silver grains were evenly distributed

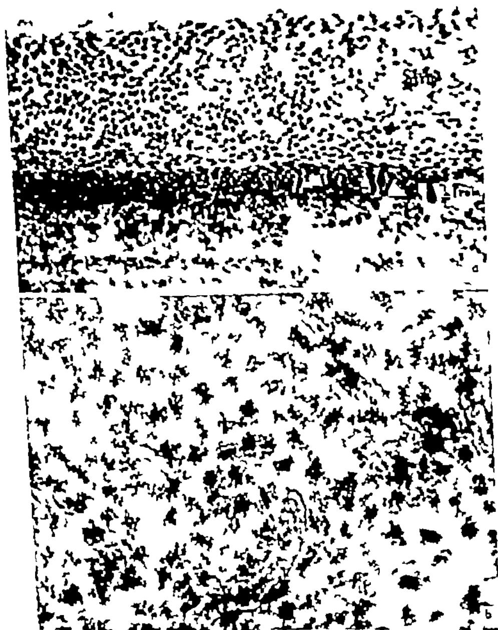


Fig. 6. ( ) The H-3-uridine utoradiograph f the lateral w ll of the guinea pig' coch-lea b the high power photograph of the box utoradiograph of the stria vascul ris.

throughout the entire stria vascularis and also throughout the spiral prominence However as is obvious from Fig 6 silver grains were more numerous on the spiral prominence than the stria vascularis. Mesothelial cells which face the scala vestibuli and the scala tympani also showed some amount of silver grains on the nucleus.

The autoradiographs obtained from the experiments of intraperitoneal administration of H-3-uridine failed to show any labels on the inner ear The dose of the isotope (0 03 mc to the guinea pig of 300 g) was too small to appear in the inner ear

COMMENTS

Hematoxylin-eosin staining and other ordinary histological methods were applied to get a clear contour of the stria vascularis in the dissected specimen However the results failed to show clear pictures owing to the fairly considerable thickness of the stria vascularis itself Phase-contrast microscopy also yielded no clear profiles of the stria vascularis with the surface view specimen

Electronmicroscopy (Smith 1957) has revealed cytological differences between the epithelium of the two regions the stria vascularis and the spiral prominence The spiral prominence cells have a more osmiophilic cytoplasm with a heavy concentration of granules In contrast the marginal cell cytoplasm has a high ergastoplasmic content as well as other membrane structures and it usually does not show microvilli on the free surface Engstrom *et al* (1955) observed at the lower border of the stria vascularis light cells appearing up to the endolymphatic surface and according to recent observations by Echandia & Burgos (1965) an apical prolongation of the limiting epithelial cell of the spiral prominence covers about half of the free surface of the most peripheral marginal cell of the stria vascularis.

The bordering cells between the stria vascularis and the spiral prominence and also between the stria vascularis and Reissner s membrane have posed an interesting question Which do they belong to the stria vascularis or the other*

Various dehydrogenases in the cochlear tissues have been examined histochemically by many investigators (Vosteen, 1956, 1958, 1960 1961 Koide *et al.*, 1962 Spoendlin & Balogh 1963 Nomura & Balogh 1964 Gerhardt 1961 Mizukoshi *et al.*, 1957 Watanuki *et al* Kakizaki 1968) Vosteen (1961) reported glutamic dehydrogenase activity in the cochlear tissues and found some considerable activity of this enzyme in the stria vascularis Dehydrogenases are contained in the mitochondria of the cytoplasm Therefore the dehydrogenase staining reveals a good contrast between the nucleus of no coloration and the cytoplasm of deep purple coloration

The autoradiography using H-3-labeled compounds permits us to make a dynamic and direct approach to the analysis of the metabolism occurring

* *la olo-l rgng 66*

in the cells and the tissues Tritium beta particles, owing to their low energy (5 69 KeV) have enabled the autoradiographic study to be the cellular level H-3-uridine is known to be a precursor for RNA in the mammal. RNA is first synthetized in the nucleus, mainly in the chromatin portion (Feinendegen & Painter 1961 Oehlert, 1961 Welling *et al* 1965) A considerably high protein metabolism of the stria vascularis was demon strated by using H-3-leucin (Plester 1960 Meyer zum Gottesberge 1961 Meyer zum Gottesberge & Plester 1961 Koburg & Plester 1962) and H-3-lysin (Koburg & Plester 1962) And a markedly high RNA metabolism was detected in the stria vascularis by Koburg (1961) using H-3-cytidine

It has been long discussed whether the exact nature of the function of the stria vascularis is secretion, resorption or both Since Corti (1851) suggested a secretory function of the stria vascularis, this secretion theory is now most prevalent (v Fieandt & Saxén, 1936 Rüedi, 19 1 Saxén, 1948 Altmann & Waltner 1950 Naftalin & Harrison 1958 Tuboi, 1960 Nomura 1961) Much structural evidence at the level of electronmicroscopy supports the function of the fluid transport of the stria vascularis especi ally it secretory function (Smith, 1957 Engström *et al* 1955 Echandia & Burgos, 1956 Yamamoto & Nakai 1964 Johnson & Spoendlin 1966 Nakayama, 1968) On the other hand, the possibility of a selective absorption i very likely in the stria vascularis. Some experimental data (Rüedi 1951 Rauch 1963) support this absorpti e function of the stria vascularis. Rauch & Ru ka (1965) and Ruska & Rauch (1967) state from their elec tronmicroscopic studies that the stria vascularis has both the absorptive and secretory functions at the same time

In this experiment H-3-uridine wa injected into the scala media and the aut radiogr ph f the stria vascularis showed a distinct incorporation of H-3-uridine into RNA This suggest that the isotope was absorbed by the m rginal cells directly from the endolymph and the RNA were synthetized in the nu leus. H wever thi study could n t rule out the route via Rei ner membrane and the perilymph of the scala vestibuli.

Electronmicroscopy (Smith 1957) re ealed many micro illi on the endo-lymphatic surface of the piral prominence cell The autoradiograph of thi study di pl yed more numerou liver grains n the spiral prominence than on the marginal cells f th stria ascularis. Lawrence (1956) observed with n th piral prominence clusters of cells appearing in the form of a rosett infiltrated by fiber which show distinct continuation with the ba ila membrane He also uggested that the clusters of "rosette cell provide a needed nutriment material to the cell of the organ of Corti. However the true function of the piral prominence is hardly known. In thi t dy there are strong indications that the epitheli l cells of the spiral prominence are more active than the marginal cell of the stria vascularis s t their resorpti e function.

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ZUSAMMENFASSUNG

Die häutigen Präparate der Stria vascularis und des benachbarten Gewebes wurden mit Hilfe der Silberreaktion, der Glutaminsäuredehydrogenase-Färbung und nach der H-3 Uridine-Autoradiographie untersucht. Zwischen der Stria vascularis und der Prominentia spiralis sowie der Reissnerschen Membran fanden sich spindelförmige Zellen auf der Endolymphseite Diese in einigen Reihen auf gestellten Zellen laufen längs der Stria vascularis von der Basis bis zum Apex. Die Autoradiographie nach Gabe von H 3 Uridin in die Endolymphe zeigte starke RNS-Synthese in der Stria vascularis und der Prominentia spiralis. Danach wurde die resorptive Funktion der Stria vascularis und der Prominentia spiralis diskutiert

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NON-EXPERIMENTAL AURAL PATHOLOGY IN RHESUS MONKEYS

(*Macaca mulatta*)

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Hearing organs of 10 rhesus monkeys (*Macaca mulatta*)—20 temporal bones—were investigated in serial sectional series with tabulation of histopathologic changes. Involvement of the middle ear and internal ear was found and propagation to the endocranium. In rhesus, the subiculum, the lid concealing in the view from the direction of the middle ear the entrance to the round window niche, was found absent (versus e.g. man). This arrangement leaves the membrane of the round window unobstructed offering direct visibility with ready access to the spaces of the membranous cochlea.

Rhesus monkeys (*Macaca mulatta* and other rhesus species) claim first place in popularity as laboratory animals, with Saimiri as strong runner up.

Most of the experimentally used monkeys belong, according to Kotera (1966), to two superfamilies with the following distribution:

Superfamily Ceboidea	Superfamily Cercopithecoidea
Family Cebidae	Family Cercopithecidae
Saimiri	Macaca
Family Callithricidae	Guenon
Marmoset	Patas
Tamarin	Baboon

In reporting on experimentation with monkeys—or with animals in general—communications enumerate provenience of the animals, procedures of histological preparation, possible artifacts developed between death and preservation but they rarely discuss their pre-experimentation status of health, or they dispose of this point with non-committal remarks such as "only healthy animals were used". Postmortem histopathological analysis is frequently neglected. In the case of the hearing organ the difficulty of histological processing of temporal bones is certainly one of the reasons.

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Thi work wa supported by Grant N XB-03319 from the Nation l Institut of Neurological Diseases nd Blindness ; Grant No 341 169 from the Central Bureau of Research, American Otological Society Grant No. 15-65 from the De fors Research Foundation.

After relevant observations on the squirrel monkey (*Saimiri sciureus* Kelemen 1966) the rhesus seemed to offer the most logical continuation along this line

MATERIAL AND METHODS

Ten monkeys, *Macacus rhesus* were obtained They were young animals, 5 males and 5 females their weight averaged 6 pounds and their body length 15 5 inches They had not undergone any previous experimental use the duration of their stay at the animal farm after their arrival there remained unknown consequently whether they arrived in an infected state or whether they acquired their diseases at the farms has not been elucidated Four died with pneumonia 4 with hemorrhageous diarrhea one was sacrificed to obtain tissues, and in one the cause of death remained unknown

After decalcification each ear was embedded in a separate celloidin block Sectioning (20 micra) was done in the horizontal plane (parallel to the main plane of the cranial base) in 17 ears, in the frontal plane in 3 ears. Besides hematoxylin-eosin several auxiliary stains were used

Histological preparation was done by Mrs Agnes Ward-Cherchian and Mrs Ruth Greulach Cherchian The photomicrograms were prepared by Mr Lloyd Matlovszky

Pathological Observations

Among the 20 middle ears 3 were completely free of infection Serous contents were present in 2 and suppuration in 6 In the internal ears 4 showed serous and 2 suppurative contents In three instances pus was seen in the internal acoustic meatus, in three instances within the meninges In one case the carotid canal contained pus, and in one an empyema of the endolymphatic sac was found

Confronting the cause of death with the autopsy findings animals dead with penumonia showed one hearing organ free of infection, one with serous, one with suppurative otitis media Those dead with hemorrhageous diarrhea showed one hearing organ free 3 with suppuration

According to single regions the following was noted

Tympanic membrane

Most conspicuous was absence of perforation in cases with middle ear suppuration In several instances the single layers were interrupted not covering each other they did not add up to a complete perforation Between the separated layers pus, an abscess was present

Middle ear

Among the 10 cases only 2 were completely free bilaterally of catarrhal or suppurative inflammatory products one third remained free at one side but showed serous secretions on the other One case showed serous



Fig. 1 Ossicle [illegible] ded by suppuratio engorgement and cellula I filtration in the tympanic mucosa membrane 46.

content in both ears another case showed serous transudate in one and uppuration in the other Five cases showed manifest suppuration in both ears thi had progressed in 2 cases to organization. The large ossicles were surrounded by pus (Fig 1) while the obturator foramen of the stapes was obliterated by purulent masses.

The pn umatic cell system shared in general the condition of the main cavities in it m stoid, tympanic and pyramidal components. Once the dura wa penetrated (Fig 2) producing uppurative meningitis.

In the inn r ear serous l byrinthitis was present in 4 ears, suppurative l byrinthiti in 2. The apical cell participated in the condition seen in the tic capsule however suppuration could "jump over the free otic capsule from the tympanic tegmen to the apical cells. Perilymphatic edema caused compres i on of th endolymphatic paces in the vestibulum in 3 ears. In 4 ears th organ of Corti remained intact amid path logical secretions. Twice Rei sner membran was pressed against the lateral cochlear wall and had caused maximal dilatation f the vestibular scala and compression of the cochlear duct Slight irregular bulging of the membrane was observed a few times, restricted to one or two turns.

Direct penetration f the infection across the oval or the round window



Fig 2 Propag tion f uppur tion from peril byri thine pneumatic cell under dura. × 16

has not been observed Along the walls of the *subarcuate fossa* hemorrhage and pus were seen in the submucous layer Pus in one case filled the *superior canal* Inside the *inner acoustic meatus* (Figs 3 and 4) exostoses had formed amid suppuration, on the walls opposite the macula sacculi In the case with the empyema of the endolymphatic sac the latter was considerably dilated

Comments on Pathology

According to Eckstein & Zuckerman (1957) rhesus monkeys may live under sheltered conditions, 30 years and more the most common and dangerous diseases contracted by them are tuberculosis pneumonia and bacillary dysentery Habermann & Williams (1957) in necropsies of 615 rhesus monkeys, designated as principal causes of death tuberculosis, pneumonia, enteritis and parasitism Knezević & Ishijima (1965) found that rhesus monkeys may become lethally infected with myobacteria for this reason they suggest the use of routine test films as a screening procedure Fiennes (1066) reported that human type tuberculosis appeared to have been eliminated from the collections of the London Zoological Garden but the bovine type always accounted for one or two deaths during the years.



Fig. 3 Suppuration in the inner acoustic meatus. 25

Lapin (1962) pointed out that the diseases which occur in monkeys during the first few months after importation are different from those developing later in animal houses.

It is rare t postulate as did House *et al* (1966) speaking of chimpanzee th t each animal should be checked for the presence of otitis media. Friedmann (1955) in isted on x ray examination of experimental animals to ex lud fr m furth r in estigati n those with radiological signs of disease.

Berberich & Kelemen (1958) described the course of acute and chronic titi media in nimals in general Haym nn (1910) and Meyer (1931) belong to the very few wh have published extensive analysis n histopathology in th m nkey ear

Th colony from which th monkeys, here reported, originated seemed t be free f tuberculosi

Conforming t human conditions, infection of the inner ear follows with medi comparatil ely rarely or if it does, the proces is "tuned d wn from a uppurative to a serous one

Anatomical Consideration

Partic ular anatomical ituations give the clue to several manifestations in pathology



Fig 4 Exostoses from the wall of the inner coustic meatus pposit the macula f the saccul × 65

Dalrymple s Atlas (1965) gives information regarding topography of the external auditory meatus in *Macaca mulatta* (see his Fig 22) Meyer con structed special ear specula (for the baboon) but even so, did not succeed in surveying the tympanic membrane in a satisfactory way

The relative infrequency of tympanic perforations, as in squirrel mon keys is not a consequence of an especially strong structure but probably of the easier drainage of the secretions through the short Eustachian tube *Conditions here prevalent may be those called by Portmann (1966)* in his classification of otitis processes otitis à tympan fermé" Tubal insufficience is cited as the possible cause when tympanic perforation does not materia lize—but in the cases here reported the cause might be the very effective *tubal drainage* As an example the rhesus *experiments* of Beck (1919) should be remembered tubal cauterization followed by sterile inflamma tion with granulations and polyps and even new bone formation behind a closed drum. This was imputed not to a high resistance of the membrane *but* as showing a different degree of vulnerability against attacks of diffe rent nature These findings should strengthen the warning not to identify absence of tympanic perforation with an intact middle ear

Pneumati ation of the temporal bone is a most influential factor in



Fig. 1. Niche f round wi dow open gainst the tympanic ca ity with wide entrance opposit the tympanic membrane; membrane of round window freely exposed. 17

dev loping pathological conditions Bast (1933) divided the tympanic cavity f the rhesus int 2 porti ns the lower or tympanum proper and the upper or recessu epitympanicus, with no definite separation between them Kirikae (1063) clas ified the accessory air spaces in man and monkey as show ing "under-developed hypotympanum and well-devel ped mastoid cells" The cavities as described by Bast form distinct entities between the group f cell th t may be called the mastoid group and the apical cluster

In marmoset the clusters of mastoid and apical cells are in wide communication with the central tympanic space and an undivided cavity is created In contra t, in rhesus the mastoid and apical cell groups are w ll def ned and so i a central pace that is, the tympanic cavity proper The ba ic difference in pathologic involvement i that in squirrel monkeys the ntire area ma toid, tympanic nd apical sections—being practically unseparated, will be simultaneou ly inv l ed by infectious processes In rhesus the 3 unit can how pathologic manifestations separately albeit all 3 part can be invaded at the same time

The tegmen, cla le intermediary f r intracranial propagation, some-t mes contain in rhesu few pneumatic cells (Fig. 2)

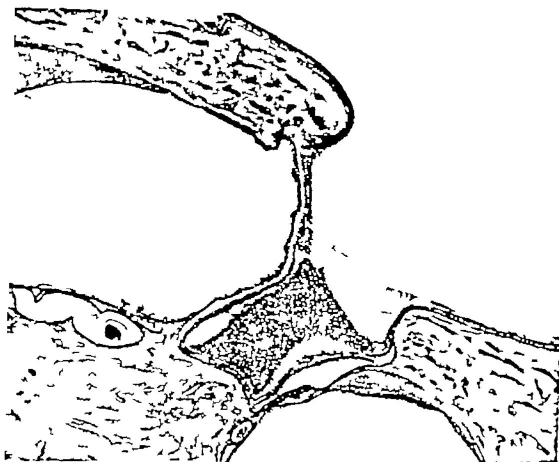


FIG. 6 Supp tion fills the nich of th round wind w membrane f rou d wind w xposed o ifice of th cochlear aquedu t nd th parall l ven u canal 30

The processus cochleariformis is, in rhesus situated dorsally above the vestibular window (Werner 1960)

The *inner ear* presents different conditions as compared with the squirrel monkey The suspension of the otic capsule within the trabecular work of the apical pneumatic cell group is not nearly so free

The cochlear capsule forms part of the osseous carotid canal This arrangement was discussed by Kelemen (1963 and 1966)

Surgical accessibility is facilitated by conditions around the niche of the round window

The spur terminating the promontory that forms an overhang in front of the round window niche, the *subiculum is lacking in rhesus* and the access from the main tympanic cavity to the niche and at its floor to the membrane of the round window is free Opposite the tympanic membrane and unobstructed the niche is open for direct approach The significance of this arrangement is obvious as, by it access to the cochlea is made comparatively easy It is not necessary as it is in man to round a spur to enter the niche and to use special devices to inspect the membrane of the round window (Figs 5 and 6)

Full exposure of the round window membrane has been illustrated by

Schall & Rambo (1948, Figs. 2 and 4) Pye & Hinchcliffe (1968) pointed out the wide differences in the mammalian middle ear between a single conti nuous cavity and a space divided by numerous bony partitions.

Nowhere i knowledge of previously present pathologic conditions in the inner ear so crucial as in the delicate experimentation regarding hearing acuity The numerous communications on this subject are lined up in the ubhuman primate bibliography of Vernon (1967) It is obvious that, in experimentation along similar lines, postmorten histopathological examina tion of the hearing organs should be postulated as a minimal control The dip in the 4000 region, of unknown origin, has been frequently found in rhesus (to this point see Kelemen, 1962)

Indubitably to reach tatistically significant data a far greater amount of material should be lined up The exigencies of the celloidin technique—nly this can be considered—limits the extension of investigations of this kind. E en so, the 20 temporals discussed constitute a sample of what one may expect to find in experimentation on the hearing organ of *Macaca mulatta*

RÉSUMÉ

Les apparells dit ires de di hésu (*Macac m latt*) c est-à-dire vi gt os temporal ont été étudié en séri sect onnelle ec la tab lation des altérati h sto-pathologiques. En ahissement de l'oreill moyen e et intern été trouvé t prop gatio d l'endocrâne D l hésus, le subiculum (le couvercle) qui g la ue d s la d rectio d l reille moyenne de l accès à la ni he d la fenêtre rond t it pa discern ble (hez l'homme c est u contraire) Dans cett insta ce la membrane d la fenêtre rond n est pas caché d nnant u visi b lité direct a ec bon accès aux espaces d la cochléa m mbran se

ZUSAMMENFASSUNG

Gehororgan on 10 Rhesusaffen (*Macac mulatt*) — 20 Schläfenbein — wurden Schnittserien untersucht und di histopathologischen Befunde ufge-ichnet Mitt lohr und I nenohr wurd lelf ch erkra kt befund n a ch mit endokranieller Fortpflanzung des path logischen Prozesses. Es konnt festgestellt werd n, dass, im Gegensat zum Menschen, beim Rhesu d s Subicul m, der k ocherne V rha g, w lcher al Fortsetzung des Promontori m der Nische des runde Fensters orgel gert ist, bwesend war Hierdurch kann die Membran des runden Fensters, vom Mitt lohr her direkt beobachtet werden u d uch der Zug g zu den Räumen der Schneck kapsel i t erleichtert.

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THE ION SELECTIVE FUNCTION OF THE EPITHELIUM OF THE MEMBRANOUS CANAL WALLS[1]

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E perime ts on an isolated canal in the living animal have shown that blocking of the vascular supply results in a decrease in end lymph pota sium concentration in this canal. In three hours of vascular block de the concentratio falls to that of the surrounding perilymph If th isolated canal has bee f lled with artifi ial perilymph d its ascular supply intact, the potassium concentration increases, indicati g a selec tive ion-transport function f the canal epithelium which, under normal conditi ns, might co tribute t maintaining the high potassium concen tration of the endolymph in the canal a well in the rest f the membranou labyri th

From clinical experience gained during fenestration operations, Meyer (19 1) concluded that the mambranous canals collapsed when perilymph wa sucked off but could regain their shape. From this experience and some experiments with animals, he arrived at the conclusion that the walls f the membranous canals were fully permeable to fluids, readily permitt ing th escape of end lymph under a mild suctional force and permitting a refilling of the canal when fluid again is supplied to the perilymphatic pace

Lempert *et al* (1934) repeated these experiments with greater precision but were unable to support Meyer s findings and therefore regarded the canal walls as impermeable They suggested that the pparent collapse f the canal was due t an optical illusion in which refraction in the fluid in the perilymphatic pace renders the membranous canal visible whereas in the absence of fluid it disappears.

Critical examination of these contradictory results gives rise to some d scus ion A long as the membranous canal is submerged in the surround ng fluid it retains it normal elliptical crossection. When perilymph is removed in mammalian pecies and the fluid surface sinks below the level f the m mbranou canal, its wall will also sink, thus flattening the canal when lifted up in air In the pigeon, however the membranous walls are thick nd more resistant Therefore they do not show the deformati n which i pron unced in the thin walled mammalian canals when perilymph i withdrawn Thi makes it evident th t this phenomenon cannot be ex plained merely an optical illusion.

[1] DRET Research Paper No. 693.

The explanation of Meyer (1951) that endolymph is removed through the canal wall is obviously not correct, as shown by Lempert *et al* (1954) These authors pointed to the high concentration of potassium in the endolymph (nearly 30 times as high as in the perilymph) and also to the extraordinarily low sodium content (only one-tenth of that in the perilymph) which could not possibly be maintained if the walls were porous As evidence against the porosity of the membranous walls of the inner ear Lempert *et al* state that the intrusion of perilymph into the endolymphatic fluid system resulting from an injury to the canal wall has a deleterious effect which produces hair cell damage. As an example they mentioned the loss of hearing following accidental injury to the canal during a fenestration operation Such a hearing loss seems to be more reasonably explained however by assuming concomitant mechanically produced cochlear damage The reason for this is as follows In two cases it has been reported to one of us (G F D) that a severe accidental injury to the canal during drilling for a fenestration resulted in temporary violent vestibular reaction but was followed by an improvement in hearing as would have been expected after a successful operation In cases where only the canal wall is damaged there are several factors which might explain why the noxious effect of perilymph sodium is restricted to the vestibular apparatus

1 It has been shown by Békésy (1952) Lawrence (1964) Konishi *et al* 1966 and others that a lesion in Reissner s membrane produces an effect on the hair cells limited strictly to the immediate vicinity of the lesion, probably due to the action of sodium-excreting elements like those found around the sensory areas in the vestibular labyrinth (Dohlman & Ormerod, 1960)

2 It is well known that the vestibular endolymphatic system is anatomically separated from that of the sacculus and the cochlea The only communication between these two systems is to be found in the very narrow utriculo-saccular ducts in which the endolymph movements from both systems are directed towards the endolymphatic duct and sac If the utriculo-endolymphatic valve has any function at all it would act as a closing mechanism when the endolymphatic pressure fails in the utricle due to escape of fluid through the damaged canal Further a membrana limitans (de Burlet) constitutes a certain barrier between the vestibular and the cochlea saccular parts, and even if this barrier is mechanically incomplete it must give some protection against minor traumatic incidents

The experiments on the permeability of the walls of the membranous canals by Meyer (1951) as well as those by Lempert *et al* (1954) were designed to investigate the possibility of gross fluid exchanges through the canal wall Meyer claimed that the canal walls acted as filters permeable to fluid of low molecular weight Due to imperfections in technique his results must be regarded as misleading as pointed out by Lempert *et al* (1954) Moreover both Meyer s and Lempert s experiments were performed



Fig. 1 ( ) A membrano canal of pigeon showi g the rich scula supply t the membranou w ll; (b) nother canal i higher magnification showi g part of the sten- h perilymphatic net ork f connecti tissu f bres.

on canal which had been removed and deprived of nutrition and oxygen supply A consid ration was given to the pos ibility of ion or water move-ments a a function of the li ing membranou walls.

On tudying the vascularization of the labyrinth, the blood supply of the membranous semicircular ca al walls gives an impression of being more abundant than would seem necessary to support only the connective tissue of the wall and the flat epithelium if no specific functi n were performed by these structures. The pattern of vascularization is well known from earlier tudies (Siebenmann 1897 Asai, 1908 Nabeya, 1923 and others) nd the impres ion of its adequacy is of course only a conjecture but pparently the function of the membranous wall has not been discu sed with regard to the possible relationship of its vascularization to the prob-lem f ion nd fluid tran fer through the canal walls.

This c mmunication therefore describes some experiments which were perf rmed on pigeon to tudy the potas ium concentration of endolymph in canal with a maintained blood supply and in canals with the blood upply excluded The anterior vertical canal (Fig. 1) is the largest of the three canal in the pigeon nd is accessible for experimental closure by cl mping at both ends. The large vessel supplying the canal from both end can be separated from the canal wall by u ing a fine needle This is, f course ry d licate operation and the possibility of damaging the vessel or impairing the blood circulation is considerable The sampling of end lymph under these condition i also difficult and some contamina-tion with perilymph must be xpected. The result of these experiments cann t therefore be regarded as a quantitative measurement of the changes in i n c ncentration in the endolymph of th canal but can give an indica-tion f the direction in which changes occur due t the experimental conditions.

EXPERIMENTAL PROCEDURE

Th pigeon wa anesthetized with intramuscular injection (2.8 ml/kg) of Equi-Thesin (mixture of chloral hydrate pentobarbital and other sub-

stances, Jensen Salsberry Laboratories, Lansing, Michigan) Following tracheotomy artificial respiration was instituted and the head was immobilized in a firm headholder The anterior vertical bony canal was exposed. The blood sinus along the convex wall of the bony canal was blocked by indenting its walls with a blunt instrument in order to get more space and to avoid accidental bleeding The bony wall of the canal was removed over a short distance close to both ends of the canal The vessels were separated from the membranous canal walls in the experiments requiring this procedure Two specially sharpened watchmaker s tweezers mounted in micromanipulators were moved down on the membranous canal embracing its walls at either end The tweezers were then closed using a clamping screw thereby occluding the membranous canal In some preparations, the blood vessels were left intact and in others the vessels were grasped together with the canal

After 1–3 hours the perilymph was removed the membranous canal wall was cut close to the tweezers and a sample of the fluid in the canal was aspirated The volume of endolymph obtained was measured, and after dilution 1000 fold with distilled water the concentration of potassium was determined directly by flame photometry

The following three conditions were studied

A Clamping the canal at both ends leaving the vascular supply intact

B Clamping the canal *and* blood vessels

C. Removing the endolymph replacing it with artificial perilymph and then clamping the canal at both ends with the vascular supply intact

RESULTS

Fig 2 shows the final concentrations of potassium in the endolymph fluid removed from the canal in each of the three experimental procedures

Considering the difficulties involved in these experiments (deformation or compression of vessels sludging of the blood etc) the analytical results cannot be expected to be precisely repeatable Nevertheless, it is clear that no appreciable change in potassium concentration in the endolymph occurs when the canal is blocked at both ends *with the vascular supply intact* (Fig 2 a) In all cases of clamping the canal *and* the vascular supply however a loss of potassium from the endolymph is apparent with time (Fig 2 b) resulting in equalization with the perilymphatic potassium concentration after 3 hours This is in accordance with the results of earlier analyses of endolymph from the cochlea or whole labyrinth in animals exposed to prolonged anoxia (Rogers, 1962 Honrubia *et al.*, 1962) Further the increase of potassium in the canal after replacement of the endolymph with artificial perilymph shows that the canal epithelium has the ability to move potassium ions into the endolymph (Fig 2 c)



FIG. 2. Graphs f result in the three groups of xperiments. Each point the graph represent the findings i separat pigeon Concentration f potassium i milliequivalent per litre i plotted gainst time in hours. ( ) Blocked ca l, vascul pply intact, (b) blocked canal d scul pply ( ) substit tion f endolymph with rtifici l perilymph, scul supply i tact.

COMMENTS

The ability to move potassium i ns selectively into the endolymph against the concentration and electrical gradients, as indicated by this investiga tion, is a function which in all probability is not restricted to the membranou canal wall. The tudies of the functional activity of Reissner s membrane by Rauch & Kostlin (1958) showed that this epithelium had the ability t transfer potassium into the endolymph from the perilymph Further in a light and electron microscopic examination of the walls of the membranous canals and estibular sacs of human temporal bones, Gussen (1966) came to the conclusi n that the vesiculations in the epi thelium and changes in the basement which she had found indicated that movement f large amounts of fluid occurred across the membranous walls. It would therefore seem surprising if the functi n of Reissner's membrane a a barrier again t sodium ion and an active carrier of potassium into the endolymph of scala media was a characteristic limited to this specific membran This would leave the rest of the endolymphatic system unprotected g inst the loss of potassium to be expected from the high concen tration gradient, which would favour a movement of potassium ions through ny membrane separating two fluid system of such great difference in ionic concentration as the endolymphatic and perilymphatic systems.

In 1962 Rogers showed by chemical analysi that the potassium and sodium concentration in the end lymph changed after the death of the nim l resulting in an equalization of the concentration of these ions in end lymph and perilymph Rogers experiments thus indicated that after cessation f the blood circulation the membranou walls as a whole behaved simple filter in contra t to the conditions found in the living nimal Recently Honrubia *et al* (1962) recorded the cochlear endolymph potential the conductance f the end lymph and the changes in potassium/sodium ratio in anoxic animals. These experiment showed that the posi tiv endolymph potential disappeared within a few minutes after the secretory and other metabolic processes ceased to function. At this point,

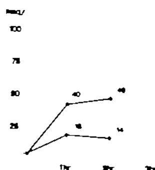


FIG 3 The change of concentration of potassium with time in an artificial perilymph solution insid an isolated section of semicircul r can l with the vascular ppl i tact.

the endolymph potential became negative corresponding to a concentration potential of the potassium and sodium content of the endolymph This negative potential declined to zero in parallel with the diffusion of the potassium and sodium ions which resulted in the equalization of their concentrations in endolymph and perilymph within three hours after the interruption of the blood supply

Thus our results on the isolated canal are in accordance with those of Johnstone s experiments In reference to the histologic studies by Gussen (1966) it therefore seems reasonable to assume that our findings on the isolated canal indicate a function of the epithelium in all membranous walls of the canals and vestibular sacs corresponding to the active potassium transport which has been shown in the cochlea with regard to Reissner s membrane (Rauch & Kostlin 1958) This ability of the membranous walls to act, in net effect as a 'potassium pump must be regarded as one link in the complex system which creates and maintains the specific ion concentration of the endolymph which has been shown to be indispensable for the function of the sensory cells of the inner ear

The function of 'pumping" specified ions in one direction must be seen in perspective The living membrane in this case the canal wall, contains capillaries, a layer of connective tissue and the inside epithelium It is a partition between two fluid systems of different ion concentrations If the vascular supply is interrupted the ions move in both directions through the partition but in greater number from the area of higher concentration toward that of lower concentration This results in an equalization of ion concentration in the two fluid systems It is well known that in any living and properly functioning partition between two fluid systems, there is always such a constant passive ion movement in both directions during normal resting conditions In order to maintain a concentration difference between the two sides of the membrane an energy consuming process must "pump" ions from the side of lower concentration into the side of higher concentration At rest this gives the general impression of an "impermeability' of the living membrane but from what has been said above it is clear that "impermeability is an inadequate expression.

The normal membranous walls of the inner ear are therefore to be regarded as partitions across which ions are constantly exchanged and actively moved. Potassium ions move passively *from* the high concentration in endolymph and they are pumped at the same rate *into* the end lymph against the high potassium gradient between endolymph on one side and all low potassium fluids on the other side such as extracellular fluids, perilymph and blood serum. This process requires energy and can therefore be fulfilled only when an adequate blood supply provides nutrition for the walls. When the ion concentration of the endolymph is reduced to that of perilymph, as in the third experimental series, the subsequent increase of potassium within the canal reveals that the "potassium pump" is indeed actively transferring potassium into the endolymph.

ZUSAMMENFASSUNG

D funktionelle Bedeutung der rganischen und elektrolytischen Kompo enten der Endolymph wird besproch n und Experimente über die Jonen-selektive F ktion der membranösen Wand des Labyrinthes werden demonst iert.

Question by Dr *H Davi* in th discus i n at th Collegium Meeti g in Chica go, Aug. 1967. Th *pri ri* expectation concerning th beh ior f the w ll of the semicircular can l i that when it ha it blood supply t is impermeable, or possibly semipermeabl but ot secr tory capable f acti tra sport. It does not show the hi t l gical structure usually associated with acti e secretion. When th ygen supply i cut ff ll membranes gradually becom totally permeable. The evidence for secretory ction is th slow slight increase in potassium f llow ing substit tion f perilymph for endolymph. The d t as presented are not complet l con in ing w thout ery caref l co trol gainst cont mi ation of the new fluid by end lymph that has not been completely insed from th mem branous ca al or from intercellular paces.

ADDENDUM

Since th rticle w s written some additional experiment have been performed on the ch nges in pota ium concentration in rtificial perilymph substituted f r nd lymph in the canal. These were done in an ttempt to further clarify the question raised by Dr H Davi in th discussion at the Collegium Meeting in Chicago, August 1967 i.e. whether the phy iological function f the canal epithelium i merely that of an impermeable barrier or actu lly to in rease the K concentration in the canal when this is *too low*. Eleven xperiment ha e been performed. Of these we wish to men tion only two, performed on pigeons showing good resistance to the con siderabl train of the operation to the animal an l the pecial tissues operated on. In these case it w pos ible to obtain three fluid samples from each pigeon during the xperiment, one h rtly fter the exchange of

perilymph for endolymph and the others one hour and two hours later The results obtained recorded in Fig 3 indicate the ability of the membranous walls of the inner ear to move specific ions against the concentration gradient Thus, this experiment suggests that in case of normal (high) potassium concentration in the endolymph the diffusional outflow of these ions is balanced by the active ion transport into the endolymph which gives the impression of impermeability" whereas in the case of a lower K concentration in the interior of the canal the outflow must be correspondingly lower and the active inward movement prevails, thereby increasing the concentration of these ions in the interior of the canal

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ELECTRODERMAL RESPONSES AND TOLERANCE THRESHOLDS FOR PURE TONES

A. EPSTEIN and H. A. SCHILL[1]

From the Clinical Audiology Laboratory Speech and Hearing Center Indiana University Bloomington Ind. U.S.A.

Electrodermal responses were utilized to determin t lera ce thresh ld for pure tones. Tones varyi g i i tensity from 70 t 120 dB SPL were presented at 4000 1000 nd 125 H respectively Result indicated that ampl tude of electrodermal responses increased with increased intensity and that responses at 1000 and 4000 Hz were consistent with previously reported subjective levels f discomfort Le els of discomfort were never reached t 125 Hz. The result suggest that mplitud of electrodermal responses may be utilized to indicate threshold f tolerance

The method used to derive the thresh lds of tolerance for hearing have been similar in most investigations (Ades *et al* 1953 1958, 1959 Fletcher & Wegel 1922 Silverman *et al* 1946 Wegel 1922) In general as the intensity f the tonal stimulus was raised, the subjects were required to indicate when a sensation other than tonal quality became evident. One of the more difficult problems facing these investigators was the quantification of the subjective response of discomfort tickle or pain" Discomfort or pain may represent different things to different individuals and may easily be confused with the quality of unpleasantness. Ades *et al* (1958, 1959) for example found it necessary to modify criteria and categories in order to obtain reasonable responses from overly cooperative subjects. Clausen *et al.* (1953 19 5) and Furer & Hardy (1950) concluded that subjects untrained in introspection were not sufficiently reliable in determining thresholds of pain

BRIEF HISTORY

Electrodermal Response

Electrodermal response (EDR) can be considered an objective measurement under certain conditions. Lacey (1947) states that physiological changes can occur for impl physical stimuli which are not intense or painful or startling, and that EDR measures f changes are objective and sensitive The response i generally considered to be an auton mic one (McCleary 1950) It has been used extensively to determine thresholds levels for young children and in cases where functional hearing loss is suspected This method of hearing testing has met with varied success for purposes noted

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intensity of the stimulus Coombs (1938) noted that strength of the EDR was related to the subject's judgment of startle but this relation was not apparent when the subject was asked to judge pleasantness or unpleasantness thus judgment of pleasant or unpleasant stimuli is inconsistent with EDR's. Clausen *et al* (1953, p 261) made the following comment concerning previous studies of pain threshold

> In all these studies the verbal report of the subject has been utilized to determine the lowest stimulus intensity which evokes a sensation of pain As it is the experience of the present authors that the verbal reports of many subject did not in any unquestionable way determine the pain threshold it is not too surprising that the verbal report should lead to difficulties when the subject is not trained in introspection.

They also state (1955) that for heat stimuli subjects often confused unpleasantness with pain and word selections for description of pain may have made it difficult to decide whether pain was really present Neverthe less, they found that verbal and electrodermal responses were comparable and that a distinct configuration of EDR was seen at pain thresholds

In the present study the EDR and, specifically the phenomenon of adaptation to that response is used as an objective measure of the upper thresholds of tolerance

EQUIPMENT AND PROCEDURE

Subjects

Seven female student nurses whose ages ranged from 18 through 20 were used as subjects The restriction of a negative history of ear pathology and hearing sensitivity better than 15 dB Hearing Level (ISO 1964) at all octave frequencies from 125 to 8000 Hz was imposed All subjects were tested in a double-walled sound insulated room.

Instrumentation

Stimulus

The output of a clinical audiometer was matched to a 35 watt power amplifier and controlled by a Hewlett Packard 350 B attenuator (Fig 1) A fuse and a 20 dB pad at the output of the amplifier served to protect the test earphone and to attenuate hum level to below audibility

Earphone

A Western Electric 705-A earphone mounted in a standard headband with dummy receiver on the opposite ear proved capable of withstanding sufficient voltage to produce levels as high as 138 dB SPL at the test frequencies. The voltages across the earphone necessary to generate 0 to

above but its use as a supra threshold measure has not been extensively investigated

Adaptation

Electrodermal audiometry (EDA) is dependent upon an unconditioned stimulus which helps to establish and maintain responses to the conditioned test stimulus One of the parameters of such a classical conditioning paradigm is adaptation which has been defined by Osgood (1953 p 78) as a progressive decrease in the intensity of sensation with continued and unvarying stimulation—this is the most general meaning of the term

Davis *et al* (1955) and Coombs (1938) have shown that adaptation occurs not only for the general test environment but also for the stimulus itself A novel stimulus, or change from what would normally be expected increased apprehension so that responses were enhanced Adaptation to the general situation was still effective though the stimulus was changed This does not preclude the possibility that responses to new stimuli could be greater than the original response if the novelty of the new stimuli is based on increased intensity Davis *et al* (1955) state that responses were greater when the intensity of the stimuli was increased which tended to override adaptation or habituation to the specific stimulus These studies did not consider randomization of stimuli levels to determine if the magnitude of response could be utilized to differentiate levels Davis *et al* (1955) hypothesized that Hull s (1949) theory of stimulus intensity dynamism" was applicable in that, as the intensity of the stimulus increased the magnitude of the response increased Hovland & Riesen (1940) randomized intensity levels and found EDR s to be linearly and positively related to the intensity of the stimulus despite randomization of presentation and position in the time continuum Furer & Hardy (1950) found that magnitude of EDR s and physical intensity of various levels of pain stimuli were positively correlated even after many trials and almost complete adaptation

It is difficult to obtain measurable EDR s for auditory stimuli near threshold without the use of conditioning but the literature suggests that adaptation does not occur as readily at relatively high intensity levels. One explanation for such a response pattern is that intense stimuli may be approaching the level of physiological tolerance for the auditory mechanism and produces a maximal response for each presentation

The measurement of auditory discomfort has been accomplished by obtaining verbal reports from listeners The evaluation of discomfort in these cases could be a combination of psychological intolerance plus the physiological factors related to bodily discomfort and stress The final level of discomfort reported by Silverman *et al* (1946) was 10 dB greater for the same subjects in subsequent tests than the initial discomfort responses. There may be a large difference between the subject s evaluation of discomfort and his actual physiological discomfort level McCurdy (1950) found that the magnitude of EDR s were related to the subjective interpretation of the

current and voltage changes in EDR s are directly related to the total effec tive electrode area. This has been defined as the total skin area wet with electrolyte whether in the form of a paste or the saline sweat moistening the skin around the electrode area. Therefore the size or area of the elec trode itself is relatively unimportant. The values obtained will be a direct function of the total area of wet skin The amount of pressure applied to maintain contact between electrode and skin can also have a direct bearing upon the measures obtained. Corn pads with a center hole of ³⁄₈ inch in diameter were filled with electrolyte and the EDR electrode was taped firmly over the center hole The corn pads thus isolated the effective elec trode area and allowed a fairly even pressure to be maintained between the electrodes and the electrolyte relative to the skin. Lykken (1959) has stated that commonly used electrolytes with a base of sodium chloride are unacceptable for resistance measurements when zinc electrodes are used because sodium chloride in contact with zinc creates ionic potential shifts which can affect measurements by as much as 100 per cent This problem is minimized if the electrolyte is of a zinc sulphate base. The formula for such an electrolyte was presented by Lykken (1959) and was used for this experiment.

Blank & Finsinger (1946) recommended that subjects be allowed to rest a minimum of 10–15 minutes prior to the beginning of an experimental session This enables them to become accustomed to the test situation and to negate the effects of prior activities upon the EDR measure A period of rest was therefore incorporated before each experimental session to con trol this variable

Preparation of subjects

The ½-inch zinc electrodes were carefully polished with fine emory paper until bright to remove ionized particles which might have affected the measurements. The subjects had been informed that they would be exposed to high int nsity pure tones. They were cautioned to make no overt responses to the stimuli and to sit as quietly as possible. The hands were washed with soap and water and the third and fourth fingers of the non-preferred hand (chosen to avoid whatever callousing might have been present on the preferred hand) were rubbed briskly with fine emory cloth and then washed with alcohol When the fingers were dry corn pads (Dr Scholl s Bev Edge felt, thick oval, no 457) with adhesive on one side were applied to the finger tips.

Ten minutes were allowed for relaxation with an additional five minutes after th test chamber door was closed. A red light alerted the subject to the initiation of th test seqn nce and remained on during the test session.

Method f p e entation

Each test session consisted f twenty four presentations of a ingle stim ulus. Neither intensity or frequency wa aried throughout the session

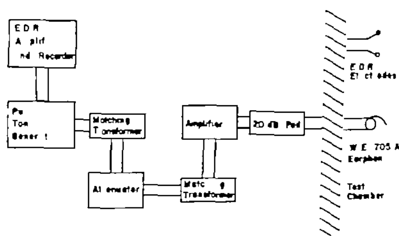


FIG. 1 Block diagram of instrumentation.

130 dB SPL at 125 1000 and 4000 Hz were measured using an NBS 9-A coupler and then checked using a Ballantine Model 300 Voltmeter prior to each experimental session At the conclusion of the experiment, coupler measures of the W E. 705 A earphone proved to be consistent with the initial measures attesting to the stability of the receiver

Electrodermal amplifier

The Grason Stadler electrodermal amplifier and recorder Model E-664 was used to control the duration of the test tone and to record responses. Stimulus duration was kept constant at one second and amplifier gain setting was constant for all subjects. The test tones had a rise-fall time of 100 milliseconds

EDR s can be evaluated on a response amplitude basis only if the gain of the electrodermal amplifier is not affected by the base resistance of the subject If the gain of the EDR amplifier changes proportionately with the changing base resistance of the subject interpretation of EDR s in terms of amplitude would be impossible Stewart (1954) in developing an instrument to detect EDR pointed out that if an infinite resistance relative to the subject s base resistance was introduced across the subject, the gain function of the EDR amplifier would no longer be affected by the base resistance of the subject. The circuitry of the Grason Stadler unit, Model E-664 is a modification of Stewart s (1954) design which made it possible for the response amplitude to be treated as a criterion measure of the EDR to various intensity levels regardless of the differences in subject base resistance (Epstein *et al.*, 1966)

Variables

Total effective electrode area

In order to measure skin resistance changes it is necessary to delineate the type and size of electrodes and the nature of the electrolyte to be used It has been demonstrated (Blank & Finsinger 1946 Lykken, 1959) that

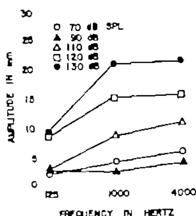


FIG. 2. A erage EDR mplitude for all subject t each frequency The parameter is the Sound Pressure Le 1 of the stim lating tone

sions. Furthermore, responses at 120 dB for the two frequencies show an almost identical relationship as that at 130 dB, although 1000 Hz followed 4000 Hz with no intervening trials Thus it is evident that order did not affect amplitude of responses.

Results obtained at 125 Hz might be related to adaptation because there is a large reduction in amplitude of responses when compared to the other test frequencies However it is more probable that those results are indicative of the effect of the stimulus upon the subjects. If the changes in amplitude f response are to be ascribed to an order effect, it would be anti cipated that additional test results following those at 125 Hz should also be affected by the order This did not occur since the inclusion of 120 dB some weeks after the conclusion of sessions nine through twelve did not affect the position one would logically ascribe to that intensity at each frequency that is between 110 and 130 dB

When the 110 dB SPL for the Western Electric Type 705-A earphone in an NBS 9-A coupler is converted to Hearing Level (ISO 1964) the following values re obtained 125 Hz–65 dB HL 1000 Hz–104 dB HL 4000 Hz–101 dB HL. The results of this study indicate that a signal at 125 Hz heard at level f 65 dB HL is not as disturbing subjectively and does not cause as great an EDR as one heard at 104 dB or 101 dB HL for the higher frequencies.

Ades *et al* (1959) in reporting results fo normal "very" hard-of-hearing and deaf ears indicate that a greater SPL is necessary to reach the subjec t e levels f feeling, discomfort and pain at 3000 Hz than at 100 Hz. The qu litative and electrodermal responses btained in thi study are not consi tent with their results.

R lation t loudness level contours

Equ l loudness contours (phons) indicate that, at Sound Pres ure Levels of 100 dB nd abov 125 1000 and 4000 Hz are perceived a pproximately

Every subject heard 70 dB SPL at 4000 Hz during the initial experimental sitting since this was considered a control and an introduction to the over all test situation During the second session either 90 110 or 130 dB SPL at 4000 Hz was used as the stimulating tone the intensity level was randomly selected for each subject. Thus, after four sessions, each subject had listened to each intensity level at 4000 Hz The same procedure was followed at 1000 and 125 Hz respectively for a total of twelve test sessions.

To prevent temporal conditioning the silent interval between stimuli was randomly varied for 45 60 75 90 105 and 120 seconds Response amplitudes which occurred within four seconds after the onset of stimulation were considered tenable and recorded

After the completion of the test runs for the 70 90 110 and 130 dB Sound Pressure Levels, each subject was tested at the same three frequencies and in the same order at 120 dB SPL. Thus each subject had fifteen test sessions the last three occurring two weeks following the end of the initial twelve sessions. All the subjects completed the testing within forty five days.

The subjects were asked to rate their initial impressions of the tone on the Coombs (1938) Scale of Affectivity and Startle They were also questioned carefully concerning their impressions of the tone in terms of numbness, touch tickle, feeling tinnitus, dizziness and discomfort

RESULTS

Response Changes as a Function of Frequency

Differences between frequencies

Analysis of variance was utilized to determine whether the amplitude of response differentiated between the level and frequency of the stimuli

A significant F value obtained between frequencies indicated that the amplitude of the EDR s did not vary an equal amount for each of the three test frequencies as the intensity of stimulation was varied A frequency by subjects analysis of variance for each level substantiated that at the Sound Pressure Levels of 70 110 120 and 130 dB significant changes occurred as frequency was changed At 90 dB the difference between responses for each test frequency was not significant

Two explanations may be entertained for the observed difference between frequencies One that the differences represent a true picture of the effects of the stimuli, and two an order effect was introduced into the experimental design because all intensities were tested at 4000 Hz initially followed by the same procedure at 1000 Hz and 125 Hz respectively Several factors tend to support the first explanation as the major reason for the differences between frequencies There is little difference in amplitude of response between 4000 and 1000 Hz at 130 dB (Fig 2) although these frequencies were separated by at least four intervening experimental ses-

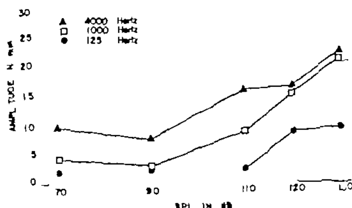


Fig. 3. Amplitude of lectrodermal respo se as function of the Sound Pressure Lev l of the stimul s. Each point on the bechas represents the mea of twenty-fou trial for seven subjects t ach intensity The parameter is the frequency f the test tone

dB SPL represents the initial threshold of discomfort. This level is consistent with the EDR s obtained except at 125 Hz (a frequency not included in the study by Silverman *et al* 1940) where no change in amplitude is noted relative to the responses for 70 and 90 dB The first marked change occurs for 120 dB and there is only a small, non-significant increase in amplitude of responses for 130 dB Stevens & Davis (1938) indicate that loudness judgments at 100 Hz increase at an accelerated rate relative to higher frequencies. The obtained EDR s show that the 70 to 130 dB SPL increase in the intensity of the stimulus at 125 Hz does not cause an increase in amplitude of response comparable to that obtained at the two higher frequencies. The subjective judgments are consistent in that 125 Hz did not affect the subjects as did the higher frequencies.

Critical differences

Critical differences were computed to determine the significance of the differences between intensities at each frequency

The increase in amplitude noted for 110 dB at the two higher frequencies was significant while significant differences in amplitude did not occur until 120 dB t 12 Hz. Th critical differences emphasize two *factors* (1) The increase in EDR amplitude varies with frequency The probability that an increase in amplitude of response will occur with an increase in intensity is greater for 1000 and 4000 Hz than for 125 Hz. (2) A sufficient increase in int nsity will cause a significant increase in EDR amplitude independent f frequency

Adaptation

Amplitud as a function f trials

Figs. 4 5 nd 6 show the result for all the subjects at each frequency over twenty-four trials. In order t mooth the curves the twenty-four

equal in loudness In the present study stimuli at 1000 and 4000 Hz do not show a significant difference in amplitude of the galvanic skin response at 120 and 130 dB SPL This is not the case for 125 Hz relative to the two higher frequencies It can be seen from Fig 3 that the response amplitude at 125 Hz is never as great as at the other two frequencies at intensities above 90 dB This factor suggests that although the high and low frequencies at these levels have been considered as equally loud exposure to 125 Hz at the three Sound Pressure Levels of 110 120 and 130 dB resulted in significantly smaller electrodermal responses than did 1000 and 4000 Hz at the same levels. This is substantiated by the subjective evaluations of startle and affectivity as well as the lack of non auditory sensations at 125 Hz which will be discussed in a later section

Effect of order upon initial responses

Examination of Fig 2 indicates that responses are greater for 70 dB than for 90 dB at 1000 and 4000 Hz. This reversal does not occur at any other intensity or frequency and may be explained by the fact that 70 dB was the first level to be presented at each frequency It is probable that apprehension as well as the novelty of the stimulus caused the larger responses at 70 dB than for 90 dB at the same frequency Had 70 dB at each frequency been randomly presented, as were the other test levels, it is probable that the reversal would not have occurred The increased amplitude for 70 dB at 1000 and 4000 Hz, therefore, is probably an artifact of the test procedure and the lack of difference between frequencies for 90 dB may be considered the result of habituation both specific and generalized, after initial exposure to a new stimulus Despite reversals at the lower intensities, it is clear from Fig 2 that responses at 4000 Hz are greater than at the other two frequencies for comparable levels It is evident that each frequency constituted a different experience for the subjects and had an important bearing upon the amplitude of response

Amplitude Changes as a Function of Intensity

Differences between intensities

It has been shown that a significant difference exists between intensities In order to determine the effects of the five intensities at each of the three test frequencies, an intensity by subjects analysis of variance was applied The F values indicated that the increase in EDR amplitude with increase in intensity of the stimulus at each of the experimental frequencies could not be considered a chance occurrence Fig 3 illustrates amplitude of response at the three test frequencies as a function of intensity It can be seen that as intensity increased above 90 dB SPL at 1000 and 4000 Hz, and above 110 dB at 125 Hz, amplitude of responses also increased

Fig 3 shows that 110 dB SPL at 1000 and 4000 Hz resulted in a marked increase in amplitude of responses. Silverman *et al* (1946) noted that 110

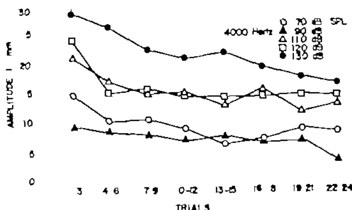


Fig. 4. Amplitude f lectrodermal responses as f nction f twenty fou trial t 4000 Hertz. The parameter is the Sound Pressure Le l f the stimulating t ne

Responses at 125 Hz for the first three trials indicate that the higher the intensity level of the stimulus, the greater the response amplitude. Adaptation occurs by trials three to six for 70 90 and 110 dB, but unlike the two higher frequencies, adaptation also occurs for 120 and 130 dB by trials nine to twelve.

Ad pt tion for the first three trials

Figs. 7 8, and 9 illustrate responses to the first three stimuli at each frequency and level It can be seen that the first three trials, and especially the difference between the first and second trials, are indicative of the course of adaptation over a larger number of trials. A large decrease in amplitude between the first and second trials indicates that adaptation will occur relatively rapidly Using this criterion, it would be predicted that ll intensities except 120 and 130 dB at 1000 Hz and 130 dB at 4000 Hz would show rapid ad ptation. When the responses over a larger number of trials (Figs. 4 5 and 6) re considered, this prediction is borne out

In general, increased intensity for the first trial is accompanied by increased mplitude of response The reversals which occur when the first three trials re grouped are minimized when the first trial is examined ndivid ally At 4000 Hz, the reversal between 70 and 90 dB is undoubtedly du to the fact that 0 dB was the first level to be presented to each subject and this would not ha e occurred had all intensity levels been randomized At 1000 Hz th reversal noted when the first three trials were grouped does n t tually occur until the third trial, indicating that examination of the first three trial individually provides the best appraisal of the effects f th timuli upon the subjects. Response amplitude was slightly greater at 125 Hz for 120 dB than for 130 dB but by the second trial the responses for 120 dB had adapted t a faster rate than for 130 dB, which would indicate that the ffect for 130 dB wa greater than for 120 dB The results ob-

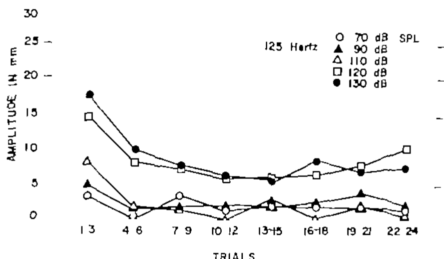


Fig 4 Amplitude of electrodermal responses as a functi n of twenty four trials at 125 H rt The param ter i the S und Pressure Level of the stimulating ton

trials were divided into eight groups of three responses each so that each point on the abscissa represents the mean of the means of three successive trials

These figures indicate that there are only small changes in amplitude of response beyond the sixth trial at all frequencies for 70 90 and 110 dB SPL If one would accept the concept of minimal changes in amplitude of response with successive trials as an operational definition of adaptation, then this phenomenon can be said to be occurring at these three Sound Pressure Levels For 130 dB SPL at 1000 and 4000 Hz there is the same rate of response decay over trials with no indication of having reached a level of adaptation by the twenty fourth trial Such an adaptation rate is evident at 1000 Hz for 120 dB SPL but not at 4000 Hz for this level The slope for 120 dB at 1000 Hz is similar to that for 130 dB but with less amplitude and with much variability of direction

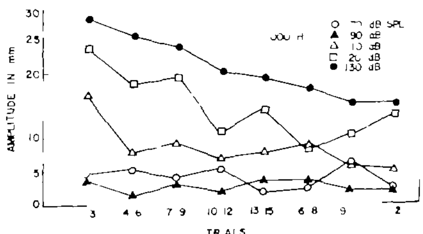


Fig. 5 Amplitude f electrode m l respo ses n f nctl n of tw t fou tri l at 1000 Hertz. Th paramete i the S u d Press re Le l of th stim l t g t

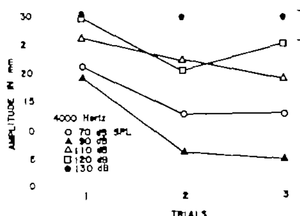


Fig. 9 Amplitude of electrodermal responses as a function of the first three trials at 4000 Hertz. The parameter is the Sound Pressure Level of the stimulating tone.

all for 90 dB at 4000 Hz. These three instances involved in one case, an affectivity rating of 4 (slightly unpleasant) and in two cases, a startle rating of three (Moderately startling). None of the subjects indicated the presence of non-auditory sensations for 70 or 90 dB at any test frequency. At 1000 and 4000 Hz for 110 dB the subjective evaluations indicated small increases from ratings for the lower intensities with some non-auditory sensations noted, especially at 4000 Hz. There were no changes in the ratings at 125 Hz for 110 dB from those obtained for lower intensity levels, nor were there any non-auditory sensations reported. The first appearance

Table 1 *Evaluation of affectivity and startle for each test level and frequency (N = 7)*

Scale of affectivity 1, very pleasant; 2, pleasant; 3, neither pleasant nor unpleasant; 4, slightly unpleasant; 5, definitely unpleasant; 6, very unpleasant; 7, extremely unpleasant. *Scale of startle* 1, not startled at all; 2, only slightly startled; 3, moderately startled; 4, very startled; 5, extremely startled.

Frequency and scale	Mean score for each sound pressure level				
	70 dB	90 dB	110 dB	120 dB	130 dB
4000 H					
Affectivity	2.9	3.0	3.9	3.7	4.9
Startle	1.3	1.7	2.7	2.6	3.6
1000 H					
Affectivity	2.1	2.7	3.7	4.0	5.3
Startle	1.1	1.1	1.9	2.7	4.0
125 H					
Affectivity	2.7	3.0	2.7	3.0	3.4
Startle	1.0	1.0	1.1	1.1	2.0

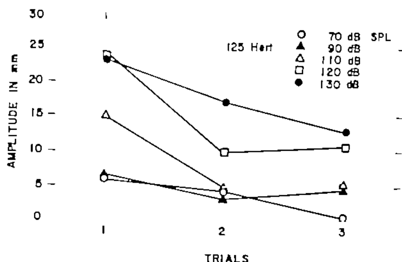


FIG 7 Amplitude of electrod rmal respon es as a function of the first three trials at 125 Hertz. The parameter is th S und Pressure Level of the stimulating ton

tained from the first three trials are in good agreement with those obtained by Hovland & Riesen (1940) and by Davis *et al* (1955) These researchers noted that an increase in the intensity of a stimulus resulted in greater EDR amplitude

Qualitative Evaluations

Each subject was asked to evaluate the stimuli subjectively on the scales of Affectivity and Startle (Table 1) suggested by Coombs (1938) as well as to describe any extra auditory sensations (Table 2) following the com pletion of the twenty four trials The subjects were asked to base their descriptions of the non auditory sensations of the stimuli upon the first two or three presentations so that factors of adaptation did not enter into the evaluation

Ratings for 70 and 90 dB were not revealing except for three instances,

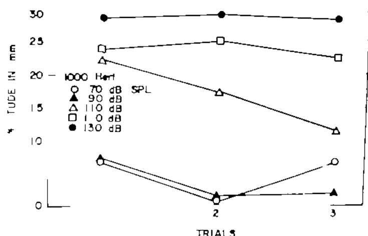


FIG. 8. Amplitud f lectrod mal re po ses f nctl f th first three trial 1000 Hertz The param ter i th So d Pres re Lev l of the timul ting t ne

for each subject over twenty four trials at each frequency and level It was concluded that

1 Electrodermal responses at 4000 Hz for each Sound Pressure Level were greater than those for comparable levels at 1000 Hz. The same was true for the relationship between the responses at 1000 and 125 Hz.

2. Amplitude of electrodermal responses increased as intensity of the signal increased

3. Electrodermal responses at 1000 and 4000 Hz supported the initial threshold of discomfort of 110 dB SPL reported by Silverman *et al* (1946)

4 The threshold of discomfort at 125 Hz was 120 dB SPL as measured by electrodermal responses. This objective measure was not in agreement with the subjective evaluations.

5 Adaptation of the EDR occurred rapidly for 0 90 and 110 dB SPL at all three test frequencies.

6. Adaptation, as operationally defined in this study was never achieved for 130 dB SPL at 1000 and 4000 Hz.

7 Subjective evaluations (ratings of affectivity and startle and non auditory sensations) at 1000 and 4000 Hz were consistent with electrodermal responses in representing the initial threshold of discomfort

8 There were no non-auditory sensations reported for any level at 125 Hz.

ZUSAMMENFASSUNG

Elektrodermale Reaktionen wurden zur Bestimmung de Toleranzschw llen für reine Tö verwendet. Tön di in der I ten ität von 70 bi 130 dB SPL variier ten, wurden j weils be 4000 1000 und 125 H präsentiert. Die Ergebnisse zeigten das die Amplitud der l ktrodermalen Reaktionen sich bei zu ehmender Inten sität ergrössert und dass Reaktionen bei 1000 und 4000 Hz mit den früher mitget ilten subjekti en Stufen des Unbehage übereinstimmten Di Stufen des U behagen wurden be 125 H nie erreicht. Die Ergebnisse weisen darauf hin, dass di Amplitud der elektrodermalen Reaktionen zu Angabe von T leran schw llen benutzt w rd kann.

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TABLE 2 *Non-auditory sensations reported for three frequencies at five Sound Pressure Levels (N = 7)*

Each row represents the number of subjects reporting the particular sensation for the level in each column.

Non auditory sensation	4000 Hz SPL					1000 Hz SPL					125 Hz SPL
	70	90	110	120	130	0	90	110	120	130	70–130
Numbness	None	None	0	3	1	None	None	0	1	4	None
Touch	None	None	0	0	1	None	None	0	1	1	None
Tickle	None	None	0	2	0	None	None	1	0	0	None
Feeling	None	None	2	3	4	None	None	0	4	5	None
Tinnitus	None	None	0	1	0	None	None	0	1	2	None
Dizziness	None	None	0	1	1	None	None	0	0	0	None
Discomfort	None	None	1	2	2	None	None	0	3	4	None

of extra auditory sensations is coincidential with the marked increase in amplitude of EDR response at 1000 and 4000 Hz as noted in Fig 3 And 110 dB is consistent with the initial levels of discomfort reported by Silverman *et al* (1946) At 125 Hz, a marked increase in response amplitude occurs for 120 dB although there were no changes in subjective evaluations from those obtained for lower intensities Since the initial increase obtained at 1000 and 4000 Hz was coincidental with the threshold of discomfort it can be hypothesized that the level of discomfort at 125 Hz is 120 dB It is evident from these results that the marked increase in EDR s along with the subjective evaluation is consistent with the thresholds of discomfort at 1000 and 4000 Hz as reported in the literature

Non auditory sensations are more in evidence at 1000 and 4000 Hz as intensity of the stimulus is increased from 110 to 120 dB There is a sharp increase of response amplitude at both frequencies from 120 to 130 dB. Fletcher & Wegel (1922) and Wegel (1922) report that the threshold of feeling lies at approximately 130 dB SPL and is close to the threshold of pain Silverman *et al* (1946) indicate that 130 dB is close to the initial threshold of tickle In the present study the preponderance of non-auditory sensations were reported as feeling discomfort or "numbness for 130 dB The fact that electrodermal responses are greatly increased at 1000 and 4000 Hz for 130 dB and that these are sustained over twenty four trials suggests that a tolerance level is being approached which is objectively in accord with the subjective evaluations

CONCLUSIONS

Tones varying in intensity from 70 to 130 dB dB Sound Pressure Level were randomly presented to seven normally hearing female subjects at 4000 1000 and 125 Hz respectively Electrodermal measures were obtained

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HISTOCHEMISCHE UNTERSUCHUNGEN ZUM EINFLUSS VON STREPTOMYCIN AUF FERMENTE DES PERIPHEREN VESTIBULARAPPARATES

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An 19 Meerschweinchen untersuchten wir histochemisch den Einfluss von 0,2 ccm einer 50%igen Streptomycinlösung, die in die Bulla der Tiere injiziert wurde, auf die Fermentaktivität des peripheren Vestibularapparates. Es zeigte sich dabei eine Abnahme der Fermentaktivität von Succinodehydrogenase, unspezifischen Esterasen, β-Galaktosidase, β-Glucuronidase und β-Glucosaminidase. Die Wirkung trat in den Strukturen der Cristae ampullares deutlicher als in denen der Maculae in Erscheinung. Die Fermentabnahme wird als Folge einer Störung des Eiweissstoffwechsels in den Zellstrukturen angesehen. Eine Zunahme der mit Sudan-B anfärbbaren Lipide deutet auf eine degenerative Stoffwechselveränderung im Sinnesepithel hin.

Bereits wenige Jahre nach der Entdeckung des Streptomycins durch Waksman (Schatz et al. 1944) und seiner Nutzbarmachung für therapeutische Zwecke konnten in der Klinik ototoxische Nebenwirkungen der Substanz beobachtet werden. Seither ist die Literatur über Streptomycinschäden des Ohres so angewachsen, dass auf eine zusammenfassende Darstellung von Eckel & Altenburger (1960) verwiesen werden muss. Durch histologische (Duvall & Wersäll, 1964), elektronenoptische (Wersäll & Hawkins, 1962; McGee & Olszewski, 1962), histochemische (Nakamura, 1957; Müsebeck & Schätzle, 1962) und elektrophysiologische (Stange et al., 1962) Untersuchungen konnte gesichert werden, dass Streptomycin in der Cochlea hauptsächlich zu einer Schädigung des Cortischen Organs und der Stria vascularis führt. Experimentelle Untersuchungen an Vestibularorganen ergaben analoge Veränderungen des Sinnesepithels von Crista ampullaris und Macula (Berg, 1951; Wersall & Hawkins, 1962; McGee & Olszewski, 1962; Igarashi et al. 1966; Spoendlin, 1966).

Auf Grund biochemischer Studien bekam man ein genaueres Bild von der Wirkungsweise des Streptomycins in den Mikroorganismen und man hat Grund anzunehmen, dass die Verhältnisse in den Zellen von Makroorganismen nicht grundsätzlich anders liegen (Moskowitz & Keller 1963). In erster Linie soll Streptomycin (S.M.) in den Zellen zu einer Hemmung

Die für die Versuche notwendigen Mengen von Streptomycin-Sulfat stellte uns dankenswerterweise Fa. Grünenthal zur Verfügung.

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Abb. 1 Crist mpullaris. N chw on SDH mit Nitroneotetraz l) Intens Reaktio m Si nesepithel, Normalbef nd. b) Schwache Reaktion, orwiegend perinucleä ach SM Vergift g. 230.

ERGEBNISSE

Ungefähr 1 2 Stunde nach Injektion der Streptomycinlösung in die Bulla zeigten di Versuchstiere eine beginnende Gang Unsicherheit, die sich in den nächsten 24 Stunden sow it steigerte da s auf eine erzwungene Lageänderu g des Körpers kaum noch Stellreflex zu beobachten waren Innerhalb der nach ten 2 Tage normalisierte sich da Verhalten der Tiere wieder so w it d ss Stellreflexe deutlich nachweisbar waren. Ein Intensitätsunterschied in den Reaktionen der verschied nen Ampullen eines Tieres oder zwischen Macula sacculi und utriculi lies sich nicht fest tellen Der N ch wei der Succinodehydrogenase ergab im Sinnesepithel der Crista ampullari am kontr llier mu senhaft blaue Farbkörnchen, die vorwiegend perinu leär ngeordnet waren (Abb 1 a) Die Intensität der Färbung gestattet nicht zu beurteilen, ob sich die beiden Haarzelltypen unterschiedlich anfär ben Im Übergangsepithel sind die Farbgranula hauptsächlich apikal angeordnet Da Ep ithel des Planum semilunatum ist ebenfall intensiv blau ngefärb t Da Bindegewebe der Crista zeigt iele Farbgranula, die beson ders in der Umgebung des Übergangsepithels auffällig werden Na h SM Vergiftung finden ich nur noch perinucleär im Sinnesepithel Anhäufungen

der Eiweisssynthese führen (Nakamura 1957 Erdös & Ullmann 1960 Flaks et al., 1962 Cox et al., 1964) möglicherweise als mittelbare Folge davon zu einer Veränderung der Membranpermeabilität (Anand & Davis, 1960 Rosano et al., 1960 Plotz et al 1961 Spoendlin 1966) und einer Fermenthemmung (Fitzgerald et al., 1948 Owen et al 1951 Peretz & Polgase 1956 Bardi et al., 1961)

Uns interessierte die Frage, ob die akute Streptomycinvergiftung die *in erster Linie zu einer Beeinträchtigung* des Vestibularorganes führt (Clorig & Fowler 1947 Fowler 1948 Barr et al., 1949) im Tierversuch eine Beeinflussung von Fermenten im peripheren Vestibularorgan erkennen lasst

METHODIK

In die Bulla von 10 Meerschweinchen injizierten wir in *Anlehnung an* Spoendlin (1966) jeweils 0,2 ccm einer 50%igen Streptomycinlosung (5 unbehandelte Tiere dienten zum Vergleich) 72 Stunden nach der Injektion wurden die Tiere in Äthernarkose dekapitiert Sofort nach Dekapitation der Versuchstiere und Herauslosen der Felsenbeine aus der Schadelbasis befreiten wir die häutigen Labyrinthanteile eines Ohres weitgehend unter dem Operationsmikroskop von ihren knöchernen Umwandungen und inkubierten in situ zur Darstellung der Succinodehydrogenase in der von Pearson (1958) angegebenen Weise Anschliessend Fixierung in Formol *Calcium nach Baker (1944) über 1 Stunde bei 4 C.* Herauslösen der drei Ampullen und Maculae Sacculi und Utriculi Einbettung in Gelatine und Anfertigung von Gefrierschnitten von *12 μ* Dicke Das Felsenbein der anderen Seite wurde zunächst 8 Stunden bei 4° C in Formol-Calcium fixiert anschliessend erfolgte Herauslösung der häutigen Ampullen und Maculae und Einbettung in Gelatine An den Gefrierschnitten wurden folgende histochemische Reaktionen vorgenommen

a) Nachweis unspezifischer Esterase nach Burstone (1957) mit Naphthol AS-D Acetat unter Kupplung an Echtblausalz RR Spezifitätskontrolle durch Weglassen des Substrates oder Zusatz von Eserin 10^{-5} m bzw Natriumtaurocholat 10^{-3} m

b) Darstellung der Galaktosidase nach Rutenburg et al (1958) mit 6 Brom 2naphthyl *β* D galactosid mit einem Zusatz von 1 m NaCl Reaktionen ohne Substrat *dienten als Kontrollen*

c) Reaktion nach Seligman et al (1954) auf *β*-Glucuronidase mit 6 Brom 2naphthyl *β* D glucuronid Kochsalzzusatz von 1 m Kontrolle *ohne Substrat* bzw Zusatz von Natriumoxalat 10^{-2} m

d) Nachweis von *β*-Glucosaminidase modifiziert nach Pugh & Walker (1958) mit Naphthol AS-LC N acetyl *β* D glucosamin Kontrollen ohne Substrat oder durch Zusatz von Natriumacetat 10⁻ m Die Farbkupplung erfolgte in *den letzten* 3 Reaktionen jeweils an Echtgranatsalz GBC

e) Lipidnachweis mit Sudanschwarz B nach Lison (1960)



Abb. 1. Crista ampullaris. Nach ... SDH mit Nitroneotetrazol. a) Intensive Reaktion im Sinnesepithel, Normalbefund. b) Schwache Reaktion, vorwiegend perinucleär nach SM-Vergift. ... 250.

ERGEBNISSE

Ungefähr 1/2 Stunde nach Injektion der Streptomycinlösung *in die Bulla* zeigten die Versuchstiere eine beginnende *Gang-Unsicherheit*, die sich in den nächsten 24 Stunden soweit steigerte, *dass* auf eine erzwungene Lageänderung des Körpers kaum noch *Stellreflexe* zu beobachten waren. Innerhalb der nächsten 2 Tage normalisierte sich das Verhalten der Tiere wieder so weit, dass Stellreflexe deutlich nachweisbar waren. *Ein* Intensitätsunterschied in den Reaktionen der verschiedenen Ampullen eines Tieres oder zwischen Macula sacculi und utriculi liess sich nicht feststellen. Der Nachweis der Succinodehydrogenase ergab im Sinnesepithel der Crista ampullaris am Kontrolltier massenhaft blaue Farbkörnchen, die vorwiegend perinucleär angeordnet waren (Abb. 1 *a*). Die Intensität der Färbung gestattet nicht zu beurteilen, ob sich die beiden Haarzelltypen unterschiedlich anfärben. Im Übergangsepithel sind die Farbgranula hauptsächlich apikal angeordnet. Das Epithel des Planum semilunatum ist ebenfalls intensiv blau angefärbt. Das Bindegewebe der Crista zeigt viele Farbgranula, die besonders in der Umgebung des Übergangsepithels auffällig werden. Nach SM-Vergiftung finden sich nur noch perinucleär im Sinnesepithel Anhäufungen



Abb. 2. Crista ampullaris. Nachweis unspezifischer Esterasen nach Burstone. *a)* Kräftige Farbreaktion im Bereich des Sinnesepithels, vorwiegend apikal, Normalbefund. *b)* Deutliche Abnahme der Farbreaktion nach SM-Vergiftung. 250

von Farbkörnchen (Abb. 1 *b*). Wahrscheinlich handelt es sich hier um Granula der Haarzellen vom Typ II. Das Übergangsepithel ist praktisch ungefärbt, während die Farbintensität im Planum semilunatum nur wenig abgenommen hat. Die Farbverteilung in den Maculae entspricht der in den Cristae. Die Abnahme der Reaktion nach SM-Vergiftung ist im Sinnesepithel der Macula allerdings nicht so ausgeprägt.

Die Befunde für unspezifische Esterase, β-Galactosidase, β-Glucuronidase und β-Glucosaminidase am Vestibularorgan des Normaltieres sind von uns schon an anderer Stelle beschrieben worden (Schätzle & v. Westernhagen 1966). Die Ergebnisse der jetzigen Untersuchungsreihe stimmen mit den bereits bekannten Befunden überein, so dass darauf verwiesen werden kann. Nach SM-Vergiftung ist eine deutliche Abnahme der Esterase-Aktivität zu erkennen (Abb. 2). Im Sinnesepithel von Crista und Macula sind nur noch apikal mehrere Farbkörnchen zu erkennen, vorwiegend in den Stützzellen und einzelnen Sinneszellen. Gelegentlich finden sich noch Farbkörnchen apikal im Übergangsepithel und diffus im Planum, das Bindegewebe und die Nervenfasern bleiben frei.

Die Galaktosidase-Reaktion ist an den behandelten Tieren im Sinnes-

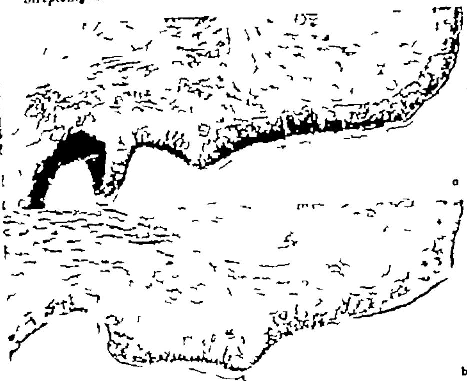


Abb. 2. Crista ampullaris, Glucosaminidase-Reaktion a) Massenhaft Farbkörnchen im apikalen Bereich des Sinnesepithels, mittlere Reaktion des Randepithels, Normalbefund. b Schwache Farbreaktion im Sinnesepithel, vereinzelt Farbkörnchen im Übergangsepithel nach SM Vergift g 350.

epithel der Cristae nur noch ganz schwach positiv etwas deutlicher im apikalen Anteil des Übergangsepithels und in den Nervenfasern Nicht ganz so hochgradig ist die Abnahme der histochemischen Reaktion in den Struk turen der Maculae

Die am Normaltier im peripheren Vestibularapparat bereits nur schwach positive Reaktion auf Glucuronidase schwächt sich nach Streptomycineinwirkung weiter ab. Im Sinnesepithel finden sich nur noch ganz vereinzelt rötliche Farbgranula, die ebenso spärlich im Übergangsepithel vorliegen. Bindegewebe und Planum semilunatum sind f st negativ Ein Unterschied in der Abnahme der Reaktion ist zwischen Crista und Macula bei der gerin gen Farbintensität nicht auszumachen.

Die intensive Glucosaminidase-Reaktion am Normaltier wird nach SM Vergiftu g so weit bgeschwächt, das sich am Sinnesepithel von Crista und Macula nur noch apikal blaue Farbgranula finden (Abb 3) Im Über gangsepithel der Crista ist die Reaktion schwach positiv das Randepithel der Macula verhält sich negativ Da Bindegewebe beider Sinnesendstellen i t neg tiv nur die Nervenfasern zeigen einzelne Farbkörnchen Die etwas



Abb. 2. Crista ampullaris. Nachweis unspezifischer Esterasen nach Burstone. a) kräftige Farbreaktion im Bereich des Sinnesepithels, vorwiegend apikal, Normalbefund. b) Deutliche Abnahme der Farbreaktion nach SM-Vergiftung. 250 ×

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Die Galaktosidase-Reaktion ist an den behandelten Tieren im Sinnes-

Macula und im Übergangsepithel der Macula finden sich zahlreiche feine schwarze Körnchen, im Übergangsepithel der Crista sind sie vorwiegend apikal angeordnet (Schätzle et al 1967) Im Planum semilunatum können die diffus verteilten Farbkörnchen meist schwer vom Pigment abgegrenzt werden Nach SM Vergiftung ist eine deutliche Zunahme der Lipidein schlüsse im Sinnesepithel und im Epithel des Planum zu verzeichnen die Farbkörnchen werden zahlreicher und grösser Besonders fällt die starke Vermehrung im Übergangsepithel auf wo nach SM reichlich grobtropfige Lipide im gesamten Zellbereich (basal und apikal) vorliegen (Abb 4 *a* und *b*)

BESPRECHUNG DER ERGEBNISSE

In unseren Versuchen führt die akute Streptomycinvergiftung im vesti bulären Labyrinth zu einer deutlichen Abnahme der Aktivität von Succinodehydrogenase unspezifischer Esterase β-Galaktosidase β-Glucuronidase und β-Glucosaminidase In erster Linie ist das Sinnesepithel weniger deut lich das Übergangsepithel, betroffen und stärker wiederum das Epithel des Planum semilunatum Das Epithel der Maculae erscheint etwas weniger empfindlich als das der Cristae Die morphologisch nachweisbaren Lipide nehmen dagegen in den genannten Strukturen nach Vergiftung deutlich zu

Um nach Möglichkeit die primären Streptomycineffekte zu erfassen, wurden die experimentellen Bedingungen so wie in der Spoendlinschen Versuchsanordnung (1966) gehalten Es wurde die lokale Applikationsform gewählt, die hohe toxische Konzentrationen am Wirkungsort verursacht und rasche Zellschädigung mit sich bringt Ein Vergleich mit der chronischen Zellschädigung durch fortgesetzte Injektion ist daher zunächst nicht möglich

Die Verteilungsmu ter am Normaltier bestätigen bereits bekannte Befunde (Schätzle & v Westernhagen 1966 Schätzle et al 1967) Für die Succinodehydrogenase konnten wir eine intensivere Reaktion beobachten als sie von Nomura & Balogh (1964) angegeben wird Die schwächere Reaktion bei Nomura & Balogh könnt darauf zurückzuführen sein, dass diese Autoren die Labyrinthe mit EDTA entkalken, ehe sie die histochemische Reaktion ablaufen lassen, während wir das knöchern Labyrinth mechan sch von den häutigen Anteilen entfernten

Die nach Streptomycinvergiftung beobachtete Fermenthemmung kann F lge einer unmittelbar am Ferment angreifenden Blockierungsreaktion sein oder ursächlich mit einer Fermentsynthese-Störung in Zusammenhang gebr cht werden

Untersuchungen über die Wi kung des SM auf den Stoffwechsel von Mikroorganismen liessen eine Hemmung der enzymatischen Vorgänge im Zitronensäurezyklus (Fitzgerald et al 1948 Hancock 1962) bzw der En doxydation (Zabos, 1960 *a*) der Diaminoxydase (Owen et al 1951 Bardi et L. 1961) und der Galactosidase (Peretz & Polgase 1956 Zabos, 1960 *b*)





Abb. 4. Crist ampullaris. Lipidnachw l mit Sudanschwarz B. Zahlreich schw rze Körn-h n im Sinnes und Überg ngsepith l im letzt ren orw g d pical. N rmalbef nd. ×400

Abb. 5. Crist ampullaris. Sud nachw rz B. Deutliche V rmehrung de schwarzen F rb-körnch n im Sinn pith l besonders im Überga gsepithel na h SM-Vergiftu g 400

inkonstante Farbverteilung im Epithel des Planum ist im Mittel auch deutlich abgeschwächt. Die schwache Farbreaktion im Wandepithel von Sacculus, Utriculus und Ampullen zeigte nach Streptomycinvergiftung keine nennenswerte Beeinträchtigung.

Am Normaltier ergibt der Lipidnachweis mit Sudanschwarz B eine intensive Schwarzfärbung der Nervenfasern. Im Sinnesepithel von Crista und

giftung im Sinnesepithel des Labyrinthes eine Zunahme osmophiler Granula, besonders in den Zellen die auch andere Anzeichen der Zelldegeneration aufwiesen.

SUMMARY

0.2 ccm of a 50% streptomycin solution were injected in the tymp nic bulla of 10 guinea pigs. By histochemical methods we studied the influence of these injection upo enzyme concentrations of peripheral vestibular structures. A decrease of enzymatic activity was observed concerning succinic dehydrogenase non-specific esterase β-galactosidase β-glucuronidase and β-glucosaminidase. This decrease was markedly higher in the elements of the crista ampullaris than in the macular structures. The loss of enzymatic activity may be explai ed by troubles of the intracellular protein-metabolism. The increase of Sudan B-stainable lipids, observed after streptomycin treatment within the sensorial nd the transitional epithelia, indicates a degenerative type f metaboli change

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erkennen. Eine Störung der Fermentsynthese nahmen bereits Fitzgerald et al. (1948) an. Peretz & Polgase (1956) und später Zabos (1960 *b*) konnten diese Synthesestörung für Galaktosidase nachweisen.

Neuere Untersuchungen ergaben als Ursache für die wachstumshemmende Wirkung des Streptomycins auf Mikroorganismen eine Blockierung der Eiweisssynthese (Chakravorty & Burma, 1962; Knippenberg et al. 1964). Dabei soll sich das Streptomycin so an die Ribosomen anlegen (Dubin & Davis 1962; Nishimura et al., 1964), dass die Anheftung der „messenger RNS" an die Ribosomen und damit die Proteinsynthese unmöglich gemacht wird (Hahn et al., 1962; Flaks et al., 1962) bzw. dass es durch Fehleinbau von Aminosäuren zur Störung der Proteinsynthese kommt.

Die Höhe der Eiweissstoffwechselrate des peripheren Gleichgewichtsapparates bestimmte Schreiner (1965) autoradiographisch. Es zeigte sich dabei, dass das Vestibularorgan einen der Cochlea (Plester 1960; Koburg & Plester 1962) entsprechend hohen Eiweissstoffwechsel aufweist. Es ist anzunehmen, dass SM im Vestibularorgan des Warmblüters, ebenso wie im Mikroorganismus, diesen Eiweissstoffwechsel blockiert. Nakamura (1957) schloss bereits von der Abnahme der proteingebundenen Sulfhydrylgruppen in der Cochlea nach Dihydrostreptomycinvergiftung auf eine Hemmung des Eiweissstoffwechsels. Auf Grund elektronenoptischer Untersuchungen sieht Spoendlin (1966) die Schädigung der vestibulären Sinnesendstellen unter SM-Vergiftung ebenso als Folge einer Störung der Proteinsynthese in diesen Zellen an. Die primäre Schädigung der Haarzellen vom Typ I wird auf eine möglicherweise besonders spezialisierte und empfindliche Proteinsynthese in diesen Zellen zurückgeführt. Spoendlin hat in seinen Untersuchungen durch parallele Applikation von 50%iger Saccharose-Lösung in die Bulla bereits eine rein osmotische Schädigung von Zellmembranen des vestibulären Apparates ausgeschlossen. Die fast gleichstarke Hemmung der verschiedensten Fermente unter unseren Versuchsbedingungen lässt auf eine nicht fermentspezifische Reaktion schliessen. Sie kann damit erklärt werden, dass von SM nicht die fermentaktiven Gruppen blockiert werden, sondern die für die Fermentsynthese notwendigen Eiweissbausteine durch den gestörten Eiweissstoffwechsel der Zelle nicht mehr zur Verfügung stehen.

Die Höhe des von Schreiner (1965) für die einzelnen Zellstrukturen ermittelten Eiweissstoffwechsels stimmt nicht mit dem Grad der von uns beobachteten Fermentabnahme überein. Diese Beobachtung kann mit der bereits besprochenen Vorstellung Spoendlins in Zusammenhang gebracht werden, dass die verschiedenen Strukturen des Vestibularorgans einen unterschiedlich differenzierten Eiweissstoffwechsel aufweisen, der gegenüber einer Streptomycinintoxikation abgestuft empfindlich ist.

Die Zunahme von Lipiden *muss im Sinnesepithel nach Streptomycinvergiftung* als degenerative Stoffwechselveränderung und Folge des Zerfalls von Zellorganellen im Sinne der Lipophanerose angesehen werden. Bereits Wersäll & Hawkins (1962) *beobachteten elektronenoptisch nach* SM-Ver-

giftung im Sinnesepithel des Labyrinthes eine Zunahme osmophiler Granula, besonders in den Zellen, die auch andere Anzeichen der Zelldegeneration aufwiesen.

SUMMARY

0.2 ccm of 50% streptomycin solution were injected in the tympanic bulla of 10 guinea pigs. By histochemical methods we studied the i fluence of these injections upon enzyme concentrations of peripheral vestibular structures. A decrease of enzymatic activity was observed concerning succinic dehydrogenase non-specific sterase β-galactosidase β-glucuronidase and β-glucosaminidase This decrease was markedly higher in the elements of the crista ampullaris than in the macular structures. The loss of enzymatic activity may be explained by troubles of the intracellular protein-metabolism. The increase of Sudan B-stainable lip ds, observed after streptomycin treatment within the sensorial nd the transl tion l epith lia, indicates d generative type f metabolic change

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FIG. 1 Retroauricular cyst before operation.

complained of a swelling behind her right ear neither painful nor tender which she had noticed one year previously This swelling was circular fluctuating, obviously cystic and not tender The external auditory canal was normal, the drumhead was somewhat lack-lustre and thickened The left side was normal Nose throat and larynx were normal

Auditory test Varied within the limits of normal on both sides for low and medium frequencies there was a marked drop for the hight on the right side (35–40 dB) The deafness was of a mixed type The X ray showed a haziness, porosity of the cell walls and an enlarged antrum on the right normal findings on the left

The patient told us the following Three years previously she felt a strong itch in the affected ear followed by a violent pain and discharge which lasted several days.

The aspiration of the contents of the cyst yielded about 6 cc of a yellow browny fluid, slightly viscous, which contained numerous brown eggs with opercules, 62 40 μ in diameter typical of *Poikilorchis congolensis* Cultures of the liquid on aerobic and anaërobic media remained sterile

All other tests performed in search of additional localisation of the parasit remained negative X-ray of the lungs was normal, repeated examinations of the sputum negative

Acta oto-laryngologica 66 444–448 (1968)

A CASE OF CHRONIC MASTOID INFESTATION BY A RARE PARASITE

(Poikilorchis Congolensis)

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The authors describe a case of a retroauricular cyst due to *Poikilorchis congolensis* This is the seventh case in the world literature After recalling the different theories which attempt to explain the mechanism of the lesion they advance the proposition that the clinical, otological and radiological picture and the findings during the operation, make it almost certain that the migration of the parasite has been through the Eustachian tube and the middle ear If one considers that all seven cases show the same localization one must conclude that this is not a coincidence and that this localization is the usual one even if the infestation in man as such may be accidental.

Vandepitte and others were the first (in 1957) to describe a new parasitic infestation occurring in the southern Congo (the Kasai province) The agent is a fluke and the lesion is a retroauricular cyst which contains pus with numerous operculated ova. In one of the four cases published the adult parasite was found It was described the same year by Fain & Vandepitte (1957) who named it *Poikilorchis congolensis* This parasite is a fluke and belongs to the family of Achillurbanidae Dolfuss. The family has two genera Achillurbania and Poikilorchis The first has two species, *A nouveli* and *A recondita* parasites of animals and not yet found in man the second has only one species, *P congolensis* found only in man

In addition to the four cases of Vandepitte *et al* it would seem that the Paragonimus cyst found by Yarwood & Elmes (1943) in a southern Nigerian man was in reality the same parasite A sixth case was observed in 1962 by Lie Kian Joe *et al* in an 8-year-old Dyak boy from Sarawak

The geographical distribution of these cases coincides frequently with the distribution of pulmonary distomatoses caused by *Paragonimus westermanni* but the absence of pulmonary pathology and a different morphology seem to indicate an infestation by a different parasite

Our case is the seventh of the series, but to our knowledge the first to go beyond the vague description of a "retroauricular cyst" and to undergo a cure through ENT investigation

The Case

Mrs N G Marie-Thérèse about 50 years of age from the Bantu tribe of Luba (southern Kasai) was first seen by us in November 1966 She

Fain & Vandepitte (1957) having seen that in some cases of pulmonary distomatosis in the Congo and the Cameroons the size of the eggs in the sputum was smaller than those of *P westermanni* and the same as those of *P congolensis* think that this new fluke is in reality also pulmonary and that this retroauricular localisation is accidental

On the other hand, the constancy of the retroauricular localisation and the absence of signs of a pulmonary localisation make us believe that the mastoid localisation in man is the rule Logically it is hardly believable as it would mean a dead end to the life cycle of the parasite

There is another hypothesis the final host of the parasite could be a different animal and not man In this case the cycle could be different and would end up with the projection of the ova outside and so insure the continuation of the species. Man in that case would only be an accidental host terminating the cycle

The cyst having a root in the mastoid cavity and a reaction of the drum head and the ossicles (causing a mild middle ear deafness) which disappeared after the operation, leads us to think that the parasite migrated through the Eustachian tube, the middle ear and the mastoid cells, causing a mild inflammatory reaction on its way

In any case we think that the *P congolensis* has a marked tendency to migrate into the human middle ear and that it can be considered as an additional agent in middle ear pathology in the tropics.

A significant fact may be that our patient has often eaten shellfish. Other authors have noticed the same fact are shellfish temporary hosts of the parasite We do not know

ACKNOWLEDGMENTS

We want to express our thanks to Prof A Giordano director of the Istituto di Anatomia Patologica of Milan University who made the histopathological examination of the cyst, and to Prof A Fain of the Institut de Médicine Tropicale of Antwerp who confirmed our identification of the parasite

We also want to thank Colonel D C. Maccahiarelli head of the Division [illegible] of the Ministero Difesa Aeronautica, Ispettorato della Sanità who made microphotographs for us in Rome

ZUSAMMENFASSUNG

Die Autoren beschreiben eine von *Poikilorchis congolensis* verursachte retroaurikuläre Zyste. Es handelt sich um den [illegible] Fall der medizinischen Weltliteratur. Zugebend, dass verschiedene Hypothesen bezüglich der Pathogenese dieser Affektion in Frage kommen, glauben die Autoren doch behaupten zu können, dass der Parasit seine retroaurikuläre Lokalisation mittels einer Wanderung durch die Ohrtrompete, das Mittelohr und den Warzenfortsatz erreicht hat. Diese Behauptung stützt sich auf die klinischen otologischen und radiologischen Zeichen wie auch auf den Operationsbefund. Sich auf die Tatsache stützend

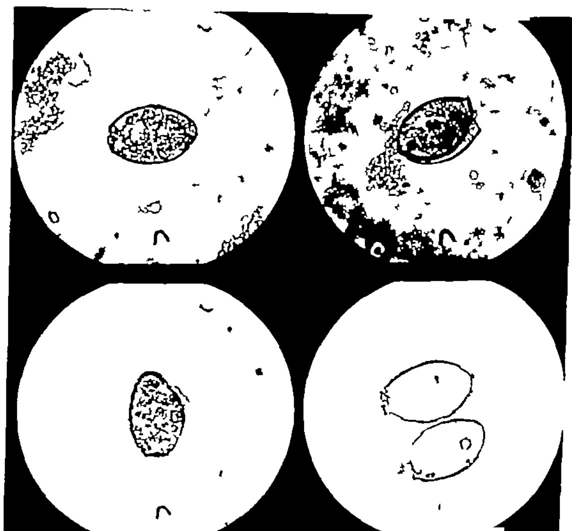


FIG 2. Ova f Polk l hl c ng l nsis f und in on patie t

Routine tests Blood tests were normal except a BSR of 66 mm/h (Westergreen) Liver and kidney functions were normal

After completion of all these tests we performed the removal of the cyst its thick (2–3 mm) and smooth walls were easily dissected from the surrounding tissues but we found that the cyst was subperiostal and plunged into the eroded mastoid antrum The intramastoid part also contained eggs of the same parasite

The histology of the cyst (Prof A Giordano) showed a thick layer of fibrous connective tissue with numerous lymphohistoid cells and Langhans giant cells Imbedded in the granulation tissue were round or oval bodies with a chitinous refringent shell, operculated enclosing either an empty space or some amorphous substance Diagnosis parasitic cyst with wall containing operculated eggs.

DISCUSSION

The rarity of the described disease explains our ignorance as to its pathogenesis or the cycle of the parasite All we can do is guess

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INFLUENCE DE L'ÉLIMINATION DES CANAUX SEMI-CIRCULAIRES HORIZONTAUX SUR LES RÉACTIONS À L'INCLINAISON CHEZ LA GRENOUILLE

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On étudie chez la Grenouille privée de la vue par la section des nerfs optiques, les réactions compensatrices à l'inclinaison du support (réactions d'origine utriculaire) avant et après section des nerfs ampullaires des canaux semi-circulaires horizontaux. 40 grenouilles ont été étudiées chez 20 d'entre elles on a coupé les nerfs ampullaires des 2 canaux horizontaux, chez 10 le nerf ampullaire droit et, chez les 10 autres, le nerf ampullaire gauche. Chez les 20 premières grenouilles nous avons noté un affaiblissement des réactions compensatrices à une inclinaison vers la droite et vers la gauche. Chez les 20 dernières, les réactions compensatrices sont affaiblies surtout lorsqu'on incline le support du côté opéré. La diminution de l'amplitude des réactions compensatrices est plus ou moins importante selon les individus (et même nulle chez certaines grenouilles). Elle n'est due ni à une lésion de l'utricule ni à une lésion du nerf utriculaire.

De très nombreux travaux ont été réalisés sur les canaux semi-circulaires horizontaux, et l'on sait que l'élimination des 2 canaux horizontaux chez un animal aveugle abolit toute réaction à la rotation autour d'un axe vertical. Dans une publication précédente (Caston 1968) nous avons montré que l'élimination fonctionnelle des 2 utricules réduisait l'amplitude des réactions lors d'une stimulation rotatoire dans un plan horizontal: nous avons voulu savoir si l'élimination des canaux horizontaux avait une influence sur les reflexes d'origine utriculaire (réflexes provoqués par une inclinaison du support autour d'un axe horizontal). A cet égard, nous n'avons trouvé dans la littérature qu'une indication peu précise, concernant l'élimination d'un seul canal horizontal (McNally & Tait, 1925): ces auteurs constatent que chez la Grenouille les réactions à la gravité sont normales après section du nerf d'un canal horizontal.

MATÉRIEL ET TECHNIQUES

L'élimination fonctionnelle des canaux semi-circulaires horizontaux a été obtenue par section des nerfs ampullaires au moyen d'un fin crochet dont la concavité était tranchante. L'ouverture de la capsule labyrinthique et la

dass die sieben bisher beschriebenen Fälle alle die gleiche Lokalisation aufweisen nehmen die Autoren an dass es sich wahrscheinlich nicht um eine zufällige, sondern um eine normale Lokalisation des Parasiten handelt, die aber möglicherweise zufällig beim Menschen vorkommt

RÉSUMÉ

Les auteurs relatent un cas de kyste retro-auriculaire dû à *Poikilorchis congolensis* Il s agit du septième cas décrit dans la littérature médicale Tout en admettant que différentes hypothèses peuvent etre prises en considération quant à la pathogénie de l affection les auteurs estiment que les signes cliniques, otologiques et radiologiques présentés par leur malade ainsi que les constatations effectuées lors de l intervention chirurgicale leur permettent d affirmer que le parasite a atteint sa localisation retro-auriculaire après migration à travers le tube d Eustache l oreille moyenne et la mastoïde Compte tenu du fait que les sept cas décrits jusqu à présent ont tous la même localisation les auteurs pensent que ceci n est probablement pas dû au hasard mais qu il s agit de la localisation habituelle d une parasitose qui est peut-être accidentelle chez l'homme

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E van V euwenhuyse D pt f Otolary g logy Lo an m U n versity Kinshasa, C go South Africa

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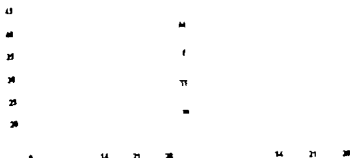


FIG. 1 (A) Réactions compensatrices à l'inclinaison. En abscisses jours comptés à partir du jour de l'opération; O grenouille engl dont l' pparell vestibulaire est intact; ordonnées aleur de l'inclinaison en degrés; la croix ( ) indique l'amplitude des réactions compensatrices de la grenouille seulement engle Trait plein inclinaison ers la gauche trait discontl inclinaison ers la droit

(B) Réactions rotatoires. En abscisses jours comptés à partir d jour de l'opération. O, grenouille engle dont l' pparell estibulaire est i tact; ordonnées mplitude de la réaction; R ucune réaction; m faible mou ement de tit ; Tf incurv tion très f ible; f faible M moyenne; F fort vec sans déplacements; la croix ( ) indiqu l' mplitude des réactions rot t ires d'une grenouille seulement engle. Trait plein rrêt d' ne rotation de sens horaire; trait discontin arrêt d' ne rot tion de sens ant horaire

la valeur de l'inclinaison est importante une extension de la patte arrière droite. Pour une inclinaison vers la gauche les réactions compensatrices sont symétriques des précédentes et ont une amplitude égale

Toutes les grenouilles étudiées présentent ces réactions mais, si l ampli tude des réactions compensatrices garde une valeur sensiblement constante chez le même animal à plusieurs jours d'intervalle, elle varie considérablement d une grenouille à une autre Il est donc indispensable d'étudier chaque nimal avant t près la section des nerfs ampullaires de façon à pouvoir établir une corrélation entre l élimination fonctionnelle des canaux horizon taux et les réaction compensatrices à l'inclinaison du support

Élimination des 2 canaux hori ontaux

Chez les 20 grenouilles que nous avons étudiées, les réactions observées à l arrêt d une rotation dans le plan horizontal sont abolies au lendemain de l'opération. Les réactions à l'inclinaison du upport ers la droite et ers la ga ch sont ffaiblies au lend main de l'opération chez 17 grenouill les Chez les 3 autre on ne note pas de modificati n sensible

En con idérant l évolution ultérieure des réactions postrotatoires, plu leurs groupes d' nimaux doi ent être envisagés

Cert in nimaux ne présentent aucune réaction rotatoire même plu leurs semaines près l'élimination f nctionnelle des canaux horizontaux (groupe I)

Chez d' utres, t ce sont les plu n mbreux, les réaction rotat ires revien

section des nerfs ampullaires sont réalisées sous un microscope opératoire Zeiss Chez quelques grenouilles, le bout central du nerf a été replié vers l arrière de façon que la réinnervation de la crête ampullaire par la régénération des fibres nerveuses soit rendue impossible (on sait en effet que chez les Amphibiens, la régénération des fibres nerveuses se fait rapidement à la température de 20–25 température qui est celle du laboratoire ou ont été menées nos expériences) Chez tous les autres animaux opérés, pour faciliter la réinnervation de la crête ampullaire le nerf une fois coupé a été laissé posé sur l ampoule du canal semi-circulaire (Gribenski 1963)

Les stimulations rétiniennes inhibant les réactions d origine vestibulaire à l arrêt d une rotation dans un plan horizontal (Caston & Gribenski, 1965) tous nos animaux ont été étudiés aveugles (la vision ayant été supprimée par la section des nerfs optiques) d abord avant la section des nerfs ampullaires, puis le lendemain de l opération ils ont ensuite été examinés toutes les semaines pendant 1 à 2 mois

A chaque étude les grenouilles ont subi les tests suivants

d une part, des rotations dans le plan horizontal dans les 2 sens, à la vitesse uniforme de 120 /s. Les réactions ont été notées à l arrêt Les rotations ont été poursuivies pendant 3 minutes de façon que l endolymphe mise en mouvement par l accélération de départ soit revenue au repos au moment de l arrêt (Gribenski, 1964) L appareil de stimulation rotatoire a déjà été décrit par Gribenski (1964)

d autre part, les grenouilles ont été basculées vers l avant et vers l arrière puis vers la droite et vers la gauche Les réactions compensatrices à l inclinaison du support ont été observées sur un plateau rectangulaire inclinable autour d un axe longitudinal Cet appareil ainsi que la technique qui permet de mesurer l amplitude des réactions compensatrices ont été décrits dans une publication précédente (Caston 1968)

RÉSULTATS

Observation des réactions che des grenouilles aveugles dont l appareil vestibulaire est intact

1) Réactions rotatoires observées à l'arrêt pour les 2 sens de rotation

A l arrêt d une rotation d une vitesse uniforme de 120 /s., l amplitude des réactions est la même chez tous les animaux la grenouille s incurve fortement dans le sens de la rotation et effectue dans ce sens, quelques sauts ou bien un mouvement de manège continu

2) Réactions à l inclinaison du support vers la droite et vers la gauche

Pour une inclinaison vers la droite la grenouille s incline du côté gauche par des mouvements le plus souvent saccadés La tête tend à rester dans un plan sensiblement horizontal La patte avant gauche se rapproche très pr s du corps alors que la droite s étend latéralement On note parfois, lorsque



FIG. 1 (A) Réactions compensatrices à l'inclinaison. *En abscisse* : jours comptés à partir du jour de l'opération. O grenouill aveugl dont l' pparell vestibulaire est intact. *ordonnées* : aleur de l'inclinaison en degrés. la croix ( ) indique l'amplitude des réactions compensatrices de l grenouill seulement a eugle. Trait plein : inclinaison ers la gauche, trait discontinu : inclinaison ers la droit.

(B) Réactions rotatoires. *En abscisse* : jours comptés à partir du jour de l' pération. O grenouille aveugle dont l' pparell vestibulaire est intact. *ordonnées* : mplitud de la reaction; R : ucu réaction; m faible mouvement de tét; *Tf* : incurs tion très faible; *f* faible; *M* moyenne; *F* fort ec ou sa déplacements; la croix ( ) indiqu l'amplitude des réactions rotatoires d'une grenouille seul ment eugle. Trait plein : arrêt d'une rotation de sens horaire; trait discontin : arrêt d'une rotation de se antihoraire.

la valeur de l'inclinaison est importante une extension de la patte arrière droite. Pour une inclinaison vers la gauche les réactions compensatrices sont symétriques des précédentes et ont une amplitude égale.

Toutes les grenouilles étudiées présentent ces réactions mais, si l'ampli tude des réactions compensatrices garde une valeur sensiblement constante chez le même animal à plusieurs jours d'intervalle elle varie considérablement d une grenouille à un autre Il est donc indispensable d étudier chaque animal avant et après la secti n des nerfs ampullaires de façon à pouvoir établir une corrélation entre l'élimination fonctionnelle des canaux horizon taux t les réaction compensatrices à l'inclinaison du support.

Elimination des 2 canaux hori ontaux

Chez les 20 grenouilles que nou avons étudiées, les réaction observées à l'arrêt d'une rotation dan le plan horizontal sont abolies au lendemain de l'opération. Les réaction à l'inclin ison du support ers la droite et vers la gau h sont ffaiblies au l ndemain d l opération chez 17 grenouilles. Chez les 3 autres on ne note pas de modification sensible

En considérant l évolution ultérieure des réactions postrotatoires, plu leur groupes d nim ux doivent être envisagés

Certain nimaux ne présentent ucune réaction rotatoire même plusieurs semaines près l'élimination fonctionn lle des canaux horizontaux (groupe I)

Chez d autres, et ce sont les plus n mbreux, les réactions rotatoires revien

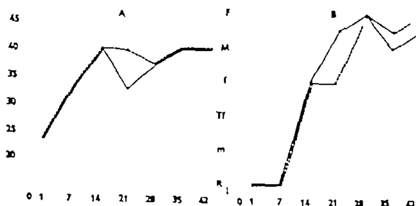


Fig. 2. (Même légende que la Fig 1)

nent petit à petit à mesure que les semaines s écoulent et au bout d un temps variable selon les animaux (de 2 à 6 semaines) leur amplitude redevient ce qu elle était avant l opération (groupe II)

Chez d autres grenouilles les réactions rotatoires reviennent, mais in complètement et n atteignent jamais une amplitude aussi grande que lorsque l animal était seulement aveugle (groupe III)

Chez d autres enfin les réactions rotatoires atteignent après plusieurs semaines, une amplitude égale à celle qu elles avaient avant la section des nerfs ampullaires, mais ceci pour un sens de rotation seulement Pour l autre sens de rotation les réactions conservent une amplitude beaucoup plus faible (groupe IV)

Nous allons successivement dans chacun de ces groupes, étudier l évolution dans le temps des réactions rotatoires et des réactions à l inclinaison du support vers la droite et vers la gauche [1]

1) Groupe I (4 grenouilles)

Les réactions à l inclinaison vers la droite et vers la gauche sont très affaiblies au lendemain de l opération par rapport à ce qu elles étaient chez la grenouille seulement aveugle l animal n effectue que de très faibles réactions compensatrices 4 semaines plus tard les réactions compensatrices restent généralement très faibles (Fig 1 A) et les réactions rotatoires toujours nulles (Fig 1 B) Chez certains animaux, l amplitude des réactions à l inclinaison du support peut être un peu plus importante (5 mm de différence de niveau entre les 2 yeux à 25) mais ne retrouve jamais une valeur normale

2) Groupe II (9 grenouilles)

Le lendemain de l opération l amplitude des réactions a une inclinaison vers la droite et vers la gauche est affaiblie Cette diminution est plus ou

[1] Les Figs. 1 A t 1 B correspond nt à un même gre uill les Figs. 2 A et 2 B à autre grenouille t les Figs. 5 A t B à n utre im l ncore

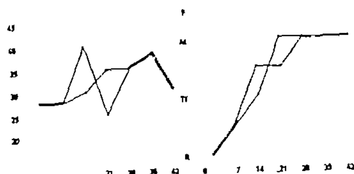


Fig. 2. (Même légende que la Fig. 1)

moins importante selon les individus. Les réactions compensatrices réacquièrent entre 1 et 8 semaines une amplitude sensiblement égale à celle observée lorsque l animal était seulement aveugle (Fig 2 A) en même temps que les réactions rotatoires retrouvent une amplitude normale (incurvation forte à l'arrêt, accompagnée de déplacements ou d un mouvement de manège (Fig. 2 B))

3) Groupe III (2 grenouilles)

Très affaiblie au lendemain de l opération l amplitude des réactions à une inclinaison vers la droite et vers la gauche redevient sensiblement normale au bout de 1 à 4 semaines (Fig 3 A) alors que les réactions rotatoires restent affaiblies une grenouille s incurve moyennement dans le sens de la rotation (Fig 3 B) l'autre très faiblement

4) Groupe IV (2 grenouilles)

a) Réactions rotatoires Grenouille n° 1 au bout de 8 semaines la grenouille à l'arrêt d'une rotation de sens horaire s'incurve fortement vers la droite et effectue quelques déplacements dans ce sens A l arrêt d'une rotation de sens antihoraire elle n effectue qu un léger mouvement de tête vers la gauche qui n affecte pas la symétrie de l animal (Fig 4 B)

Grenouille n° 2 8 semaines après l opération la grenouille s'incurve fortement vers la gauche à l arrêt d une rotation de sens antihoraire et effectue un mouvement de manège dans ce sens A l arrêt d'une rotation de sens horaire l'animal ne s'incurve que très faiblement vers la droite (Fig 5 B)

b Réaction à l'inclinaison vers la droite et vers la gauche Grenouille n° 1 L amplitude des réactions compensatrices, après avoir baissé considérablement le lendemain de l opération réacquiert petit à petit au bout de 8 semaines, une valeur un peu plus importante mais qui n est jamais égale à celle notée avant la section des nerfs ampullaires (Fig. 4 A) Les réactions reviennent à peu près symétriquement pour les 2 sens de l'inclinaison

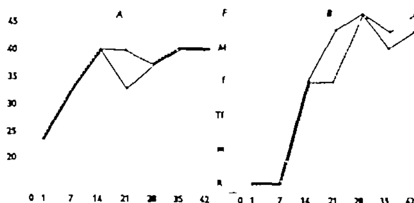


Fig 2 (Mêm légende que la Fig 1)

nent petit à petit à mesure que les semaines s écoulent et au bout d'un temps variable selon les animaux (de 2 à 6 semaines) leur amplitude redevient ce qu elle était avant l opération (groupe II)

Chez d autres grenouilles les réactions rotatoires reviennent, mais in complètement, et n atteignent jamais une amplitude aussi grande que lors que l animal était seulement aveugle (groupe III)

Chez d autres enfin les réactions rotatoires atteignent après plusieurs semaines, une amplitude égale à celle qu elles avaient avant la section des nerfs ampullaires mais ceci pour un sens de rotation seulement Pour l autre sens de rotation, les réactions conservent une amplitude beaucoup plus faible (groupe IV)

Nous allons successivement dans chacun de ces groupes, étudier l évolu tion dans le temps des réactions rotatoires et des réactions à l inclinaison du support vers la droite et vers la gauche[1]

1) Groupe I (4 grenouilles)

Les réactions à l inclinaison vers la droite et vers la gauche sont très affaiblies au lendemain de l opération par rapport à ce qu elles étaient chez la grenouille seulement aveugle l animal n effectue que de très faibles réactions compensatrices 4 semaines plus tard les réactions compensatrices restent généralement très faibles (Fig 1 A) et les réactions rotatoires tou jours nulles (Fig 1 B) Chez certains animaux l amplitude des réactions à l inclinaison du support peut être un peu plus importante (5 mm de diffé rence de niveau entre les 2 yeux à 25) mais ne retrouve jamais une valeur normale

2) Groupe II (9 grenouilles)

Le lendemain de l opération l amplitude des réactions à une inclinaison vers la droite et vers la gauche est affaiblie Cette diminution est plus ou

[1] Les Figs. 1 A et 1 B correspo d nt à une mêm gre lll les Figs. 2 A et 2 B à utre grenouill etc les Figs. 5 A et 5 B à un utre nim l core

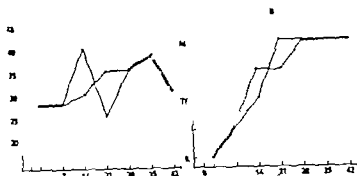


Fig. 2. (Même légende que 1 Fig 1)

moins importante selon les individus. Les réactions compensatrices réacquièrent entre 1 et 8 semaines une amplitude sensiblement égale à celle observée lorsque l animal était seulement aveugle (Fig 2 A) en même temps que les réactions rotatoires retrouvent une amplitude normale (in curvation forte à l'arrêt, accompagnée de déplacements ou d un mouvement de manège (Fig 2 B))

3) Groupe III (2 grenouilles)

Très affaiblie au lendemain de l opération, l amplitude *des réactions à* une inclinaison vers la droit et vers la gauche redevient sensiblement nor male au bout de 1 à 4 semaines (Fig. 3 A) alors que les réactions rotatoires restent affaiblies une grenouille s'incurve moyennement dans le sens de la rotation (Fig 3 B) l autre très faiblement

4) Groupe IV (2 grenouilles)

a) Réactions rotatoires Grenouille n° 1 au bout de 8 semaines la *grenouille* à l arrêt d une rotation de sens horaire s'incurve fortement *vers la* droite et effectu quelques déplacements dans ce sens. A l'arrêt d une rotation de sens antihoraire elle n effectu qu un léger mouvement de tête vers la gau he qui n affecte pas la symétrie de l animal (Fig 4 B)

Grenouille n 2 8 semaines après l'opération *la grenouille* s'incurve fortement ers la gauche à l arrêt d'une rotation de sens antihoraire et effectue un mouvement d manège dan ce sens. A l arrêt d une rotation de sens horaire l'animal ne s'incurve que très faiblement vers la droite (Fig. 5 B)

b) Réaction à l'inclinais n vers la droite et vers la gauche Grenouille n 1 l mplitude des réactions compensatrices, apres avoir baissé con sidérablement le *lendemain de l opér tion*, réacquiert petit à petit, au bout de 8 semaines, un valeur *un* peu plu importante mal qui n est jamai ég le à celle n tée av nt la section des nerf ampullaires (Fig. 4 A) Les réactions reviennent à peu près symétriquement pour les 2 sen de l'inclinaison.

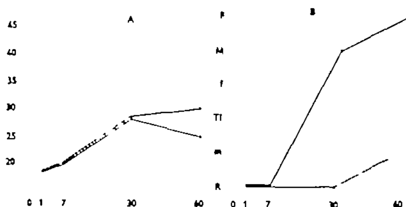


Fig 4 (Même légende que la Fig 1)

Grenouille n 2 Au bout de 2 mois les réactions compensatrices sont ce qu elles étaient avant l opération (Fig 5 A) mais on note une légère dis symétrie entre l amplitude des réactions pour une inclinaison vers la droite et vers la gauche les réactions pour une inclinaison vers la droite sont un peu plus importantes que celles observées pour une inclinaison vers la gauche

Ce résultat nous a conduit à réaliser une seconde série d expériences sur 20 grenouilles chez lesquelles un seul canal horizontal a été supprimé chez 10 d entre elles le canal horizontal gauche chez les 10 autres, le canal horizontal droit

Elimination du canal hori ontal gauche

1) Réactions observées à l'arrêt de la rotation le lendemain de la section du nerf ampullaire

a) Arrêt d'une rotation de sens horaire Les réactions sont très affaiblies par rapport à ce qu elles étaient avant l opération L animal n effectue qu un faible mouvement de tête vers la droite ou bien s incurve très faiblement dans ce sens.

b) Arrêt d une rotation de sens antihoraire Chez 8 grenouilles, l ampli tude des réactions est la même avant et après la section du nerf ampullaire l animal s incurve fortement vers la gauche et effectue dans ce sens quel ques déplacements ou bien un mouvement de manège continu Chez 2 ani maux, les réactions sont légèrement plus faibles et se traduisent par une in curvation vers la gauche moyenne ou assez forte qui n est jamais suivie de déplacements.

2) Réactions compensatrices après élimination du canal

Le lendemain de l opération on observe chez 5 grenouilles une diminu tion de l amplitude des réactions à l inclinaison vers la gauche Cet affai blissement des réactions est plus ou moins important selon les animaux

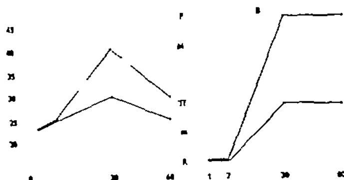


FIG. 5 (Même légende que l. Fig. 1.)

Plusieurs semaines après l'opération ces grenouilles réacquièrent des réactions compensatrices d'amplitude identique à celle observée avant l'opération (Fig. 6 A) en même temps que les réactions postrotatoires dirigées vers la droite redeviennent normales (incurvation forte vers la droite suivie de déplacements ou d'un mouvement de manège (Fig. 6 B).

Une 13ième grenouille dont les réactions compensatrices et rotatoires, au lendemain de l'opération étaient les mêmes que chez les animaux précédents, est morte quelques jours après l'opération.

Parmi les 4 dernières grenouilles, 2 présentent dans leurs réactions, une modification inverse des précédentes (réactions compensatrices normales pour une inclinaison vers la gauche, très fortement diminuées pour une inclinaison vers la droite); les 2 autres ont leurs réactions affaiblies pour les 2 sens de l'inclinaison. Plusieurs semaines après l'opération ces 4 grenouilles présentent toujours des réactions postrotatoires dirigées vers la droite faibles et même très faibles. Les réactions compensatrices ont retrouvé une amplitude normale chez 2 d'entre elles. Les 2 autres ont conservé à l'inclinaison des réactions de faible amplitude.

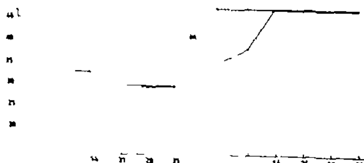


FIG. 6. Même légende que la Fig. 1.)

Les Figs. 6 A et 6 B correspondent à une même grenouille.

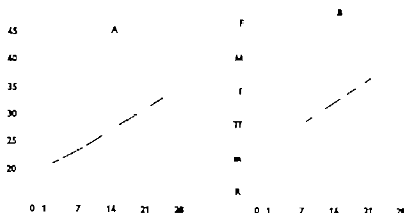


Fig 7 (Même légende que la Fig 1)

Elimination du canal horizontal droit

1) *Réactions observées à l arrêt de la rotation*

Le lendemain de la section du nerf ampullaire

a) Arrêt d une rotation de sens horaire Les réactions, chez 9 grenouilles, sont identiques à celles observées avant l opération (incurvation forte vers la droite suivie de déplacements ou d un mouvement de manège) Une grenouille s incurve assez fortement vers la droite sans jamais se déplacer

b) Arrêt d une rotation de sens antihoraire L amplitude des réactions est considérablement affaiblie par rapport à ce qu elle était avant l opération 2 grenouilles n ont plus aucune réaction 5 autres effectuent un très faible mouvement de tête vers la gauche (ce mouvement n affecte pas la symétrie de l animal) les 3 derniers animaux s incurvent faiblement vers la gauche

Plusieurs semaines après l opération

Les réactions rotatoires dirigées vers la gauche retrouvent une amplitude normale chez 5 grenouilles 2 à 4 semaines après la section du nerf ampullaire Chez 2 autres grenouilles les réactions reviennent incomplètement (incurvation moyenne vers la gauche) et enfin chez 2 autres animaux les réactions postrotatoires dirigées vers la gauche sont restées très faibles 4 semaines même après l opération La dixième grenouille, morte quelques jours après l opération n a pu être étudiée

2) *Réactions à l inclinaison vers la droite et vers la gauche*

Le lendemain de la section du nerf ampullaire, chez 4 grenouilles les réactions compensatrices ne sont pas sensiblement modifiées leur amplitude est la même qu avant l opération Chez 4 autres grenouilles, l amplitude des réactions compensatrices à une inclinaison vers la droite est fortement diminuée pour une inclinaison vers la gauche, leur amplitude est sensiblement la même qu avant l opération Une grenouille montre dans ses réactions, une modification inverse des précédentes affaiblissement des réactions pour une inclinaison vers la gauche réactions normales pour

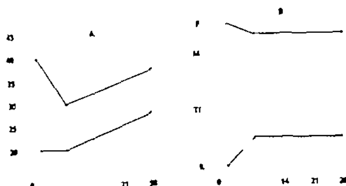


Fig. 8 (Même légende q   la Fig. 1)

une inclinaison vers la droite La dernière grenouille enfin a des réactions affaiblies pour les 2 sens de l'inclinaison   ces réactions sont cependant beaucoup plus amoindries pour une inclinaison vers la droite que vers la gauche

Plusieurs semaines après l opération, 3 grenouilles retrouvent des réac tions compensatrices d amplitude normale Chez 2 animaux, les réactions ont conservé une amplitude faible bien qu un peu plus importante qu au lendemain de l opération

3) C mparaison entre les réactions rotatoires et les réactions compensatrices pr s la secti n du nerf ampullaire

3 grenouilles retrouvent des réactions normales ou presque normales (in curvation forte ou moyenne vers la gauche) à l arrêt d une rotation de sens antihoraire en même temps que l amplitude des réactions compensatrices a une inclinaison latérale redevient sensiblement égale à celle notée avant l'opération. Le parallélisme entre la réapparition des réactions rotatoires dirig es vers la gauche et celle des réactions compensatrices est très apparent ici comme d n le cas de la uppression du canal horizontal gauche La Fig 7 en d nne un exemple chez une de ces grenouilles. Deux animaux ne présentent toujours, plu ieurs semaines après l'opération, que des réac tion rotat ires dirigées vers la gauche d'amplitude faible les réactions compensatrices à une inclinaison ers la droite conservent aussi une ampli t d f ible (Fig 8)

DISCUSSION ET CONCLUSION

I R acti ns rotatoire

a) l'limination de   canaux horizont ux Nous avon vérifié que la é p rition progressive des réactions rotatoires était liée à la régénération

Les Figs. 7 A et 7 B correspondent à ne même grenouille les Figs. 8 A et 8 B à tre grenouill

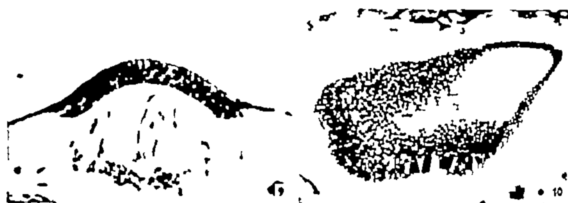


Fig 9 Crêt ampullaire d un canal horizontal, 4 semaines après la secti d n rf ampullaire Les fibres nerv uses ont régénéré et la crêt a une structure n rmale (coupe horizontale)

Fig. 10 Macule utriculaire 6 semaines après l section du nerf mpullaire d canal horiz ntal La macul a une structure normale (coupe h l ontal)

des nerfs ampullaires qui vont réinnerver la crête de l ampoule des canaux horizontaux. Par dissections nous avons montré que les nerfs n avaient pas régénéré chez les grenouilles qui n avaient retrouvé aucune réaction rota toire Ils avaient régénéré en entier ou en partie chez les animaux dont les réactions rotatoires étaient redevenues normales Chez quelques unes de ces dernières grenouilles l étude de coupes histologiques[1] nous a permis de vérifier que la crête ampullaire et le nerf qui l innerve étaient en bon état l image étant semblable à celle observée chez une grenouille normale (Fig 9) Chez les 2 grenouilles du groupe IV seul le nerf ampullaire gauche avait régénéré chez la grenouille n 1 le droit chez la grenouille n 2

b) Elimination d'un seul canal hori ontal Les réactions dirigées vers le canal intact reviennent plus ou moins complètement La réapparition totale de ces réactions est liée à la régénération du nerf observée comme précédemment par dissections et sur coupes histologiques. Chez quelques grenouilles, les réactions rotatoires restées faibles sont cependant plus importantes qu au lendemain de l opération nous avons vérifié chez ces animaux que le nerf ampullaire n avait pas régénéré Il s agit dans ce cas, d un phénomène de compensation (Gribenski 1955 1957)

2) Réactions a l inclinaison du support

Les réactions compensatrices sont généralement affaiblies apres l opéra tion. Cet affaiblissement est plus ou moins important selon les animaux et est même nul chez certains d entre eux

Lorsque les réactions rotatoires ne réapparaissent pas au bout de plu sieurs semaines les réactions à l'inclinaison du support restent affaiblies (Figs 1 et 8) Lorsque les réactions rotatoires reapparaissent les réactions

[1] L'inclusi n des oreilles ét f it pa l méthod mi t collodi paraffin Les coupes, d 10 μ ont été colorées à l'hémalun-éosi

compensatrices réapparaissent également et le parallélisme entre ces 2 phénomènes est bien visible sur les Figs 2 6 et 7

Chez les grenouilles privées d un seul canal horizontal, les résultats semblent montrer que les réactions compensatrices sont affaiblies surtout lorsque l'inclinaison se produit vers le côté opéré (Figs. 6, 7 8)

Par dissections nous avons vérifié que le nerf utriculaire était intact et les coupes histologiques nous ont montré une image de la macule utriculaire semblable à celle observée chez un animal normal. Aucun signe de dégénérescence n a été noté (Fig 10) Mais ces observations ont été faites plusieurs semaines après l opération et l on peut se demander si le nerf utriculaire qui aurait pu être lésé lors de la section des nerfs ampullaires aurait ensuite régénéré sa partie périph rique. Cependant, la section du nerf ampullaire d'un canal horizontal est une opération assez simple qui lorsqu elle est réalisée soigneusement, ne touche ni la macule ni le nerf utriculaire D autre part, lorsque la grenouille se réveille après l'opération, elle ne présente aucune position forcée. Son attitude est celle d une grenouille normale Or nous avons pu vérifier de nombreuses fois que le moindre mauvais traitement infligé à l'utricule se traduisait immédiatement sur la posture de l animal, celui-ci adoptant une position dissymétrique avec inclinaison du côté opéré Cette dernière observation nous permet d affirmer que ni le nerf utriculaire, ni la macule n ont subi de lésion

En conclusion on peut dire que l élimination fonctionnelle des canaux semi-circulaires horizontaux, chez la Grenouille, provoque, en général, une diminution plus ou moins importante des réactions d origine utriculaire L élimination l ilatérale des canaux horizontaux provoque une chute des réactions à l'inclinaison du support, à la fois vers la droite et vers la gauche L élimination d un seul canal horizontal semble déterminer un affaiblissement des réaction lorsque le support est incliné du côté opéré

N u essaierons, dan un prochain tra ail, de sa oi quelle est la nature des relations qui existent entre l'appareil ampullaire et l appareil utriculaire

SUMMARY

W have st died the compensat g reaction elicited by tilting (reaction herted by the utricules) in th frog, blinded by secti n of optic nerves, before and fter section of th ampullar nerves of th horizont l semi-circular canals. Fort frogs ha been tudied 20 f them the ampullar nerves f th horizontal nal have been cut bilaterally i 10 f them we cut the right mpulla nerv d in the other 10 the l ft mpullar nerve In the first 20 frogs reduct on of the compensating reactio licited by tilting t the right and to the left side has been noted I the othe 20 the compensating reaction are reduced especially when the tilt-table i tilted t ward th operated side Th reducti n of amplitude f the compensating reaction l more or less import nt according to th individual frog (there i a l ible reduction in some frogs) It i due n liber t a lesion f th ut icule nor t the utricular erve

ZUSAMMENFASSUNG

Am Frosch der das Sehvermögen durch den Durchschnitt des optischen Nerven verloren hat wurden die ausgleichenden Reaktionen gegenüber der Neigung der Stütze (*Utrikularreaktion*) vor und nach dem Durchschnitt der Ampullarnerven der halbzirkularen horizontalen Kanäle studiert 40 Frösche wurden beobachtet bei 20 von ihnen haben wir die Ampullarnerven der 2 horizontalen Kanäle durchschnitten bei 10 den rechten Ampullarnerven und bei weiteren 10 den linken Ampullarnerven Bei den 20 ersten Fröschen haben wir eine Schwächung der Kompensationsreaktionen bei einer Neigung nach rechts und nach links festgestellt. Bei den letzten 20 sind die Kompensationsreaktionen geschwächt, besonders wenn wir die Stütze gegen die operierte Seite neigen Das Abnehmen der Weite *der Kompensationsreaktionen ist mehr oder weniger wichtig, je nach den* Individuen (und bei gewissen Fröschen sogar nicht wahrnehmbar) Es hat seine Ursache were in einer Utrikalverletzung noch in einer Verwundung des Utrikullarnerven

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A QUANTITATIVE STUDY OF THE EFFECT OF THE ACOUSTIC STAPEDIUS REFLEX ON SOUND TRANSMISSION THROUGH THE MIDDLE EAR OF MAN

E. Borg

From The Department of Physiology Karolinska Institutet Stockholm Swed n

The influence on sound transmission through the middle ear as exerted by th coustic stapedius muscle reflex, has been investigated in subjects w th unilateral peripheral facial paralysis of short duration. Reflex activity in both ears was recorded simultaneou ly as a change in th acoustic impedance at 800 cps. Bursts f pure t nes between 300 and 3000 cps were used t eli it this refl x. The influen e of the stapedius reflex o the tra smission of the sound stim lus through the middle ear wa btained from measurements made during paralysis and after com plet recovery The amplitude of the crossed reflex (recorded as an imped nce change) was used s a relati e measure of the excitation in the cochlea on the affected id The magnitud f th influence on the transmission of the stimulus tone was btained from the shift of the stimulus response curve of the crossed reflex which was caused by the stapedius reflex fter reco ery Attenu tion was found t be greater at frequencies below th resonant frequency f the middle ear (about 1000 cps) than abo e A pure t of …00 cps (20 dB abo e reflex threshold) was ttenuated 12–15 dB wherea tone f 1450 cp (16 dB above threshold) was atte uated 0–6 dB. After the recovery of stapedius function, the excitation in the cochlea reached a maximal level (at 500 cps, 11 dB SPL) whi h wa lower than during palsy This decrease in maximal itation w interpreted as sh wing that "perfect regulatory ffect I erted b the stapedius reflex in go erning sound transmission through th middle ear wh n th reflex is ear its maximal degree f acti ty A con ivable planation for the incre sed mplification in the feed-back circuit is that a strong tapedius contractio might hange the mod of vibration of the stapes and thus diminish the energy transmitted t th cochlea. The oscillati i th mplitude f the impeda ce ha ge as licited by low frequ cy stimulation, were shown t be due t the ll ity of th st pedius of the stimulated sid

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Th influence on sound transmission through the middle ear as exerted by the acoustic stapedius muscle refl x has been in estigated i subjects with unilateral peripheral facial paralysis of short duration. R flex activity in both ears was recorded simultaneou ly as change in the acoustic impedance at 800 cps. Bursts of pure t nes between 300 and 1000 cps were used t elicit this reflex. The influence f the stapedius reflex on the transmission f the sound stimulus through the middle ear wa obtained from measurements made during paralysis and after om- plete recovery The amplitude of the crossed reflex (recorded as an impedance change) was used as a relative measure of the excitation in the cochlea on the affected sid Th magnitud f the influence on th transmission of th stimulus tone was btained from the shift f th stimulus response curve of the crossed reflex which was caused by th stapedius reflex fter recovery Attenuat on was found to be greater t frequencies below th resonant frequen y of the middle ear (about 1000 cps) than abo A pure tone of 500 cps (20 dB abo e reflex threshold) was attenuated 12 15 dB wh reas ton of 1450 cp (16 dB abo e threshold) was attenuated 0–6 dB. After the recovery of stapedius func- tion, th e citation in the cochl reached maximal level (t 500 cps, 11 dB SPL) whi h was lower than during palsy This decrease in ma mal tation was interpreted as showing that "perfect regula- tory effect erted by the stapedius reflex in governing sound trans- mi sion through the middle ear when th reflex is near its maximal degree of act vity A conceivable explanation for the increased ampli- fication in th feed-ba k circuit is that a strong staped us contracti n might change the mod of ibration of the stapes and thus diminish th nergy transmitted t th cochlea. The oscillation i th mplitude of the mpedance change as licited by low frequ ney stimulation, wer shown t be due t the ctivity f the stapediu of the stim lated sid

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A loud sound stimulation of one ear elicits a contraction of the middle ear muscles f both ears. This acoustic reflex in man activates only the stape- dius muscl (Jepsen, 1955) Most of the available data on the effect of the

muscle contraction on the sound transmission are from animal experiments (Wiggers, 1937 Wever & Bray 1942 Wever & Vernon 1955 Simmons, 1959 Galambos & Rupert 1959 Møller 1965) *In man, most of these* studies have been performed using psychoacoustic methods (Perlman, 1938 Jepsen 1955 Shapley 1954 Loeb & Riopelle 1960 Reger 1960 Ward 1961 Fletcher & Loeb 1962 Hansen 1965) In addition direct measurements on postmortem temporal bones have evaluated the effect on sound transmission by artificially applied forces to the middle ear structures (Neergaard *et al* 1963 Elpern *et al.*, 1965)

The relationship between the degree of stapedius reflex activity (expressed by the intensity of the reflex eliciting tone) and the attenuation of sounds of different frequencies has not been investigated with direct methods in living man In this study impedance measurements on patients with unilateral Bell s palsy (with stapedius paralysis of short duration) were used to investigate the influence of the stapedius reflex on the transmission of intense sound

METHOD AND MATERIAL

The apparatus and the procedure for bilaterally recording the acoustic impedance change caused by the middle ear reflex was the same as that described by Møller (1961 *b*) The measuring devices were hermetically sealed to the ear canals by a dental molding substance (Lastic 55) The "measuring tone (800 cps, 65 dB SPL) and the tone eliciting the reflex *activity i e the stimulus tone were electrically balanced out* The stimuli were then presented in alternating succession to the left and the right ear Tone bursts of 1000 msec duration (the rise time to 90% of maximal amplitude and the decay time to 10% was 2 msec) in the frequency range between 300 and 3000 cps were used to elicit the reflex. The stimuli were presented with varying intervals and the intensity was increased in steps of 2 or 4 dB from below threshold to the maximal intensity used and then stepwise lowered to below threshold Thus two determinations were made at every intensity tested The sound pressure was measured in each experiment instead of relying on a standard calibration These individual measurements were made to avoid errors in the determinations of the sound pressure level due to individual anatomical differences of the ears and variations in the position of the stimulation devices in the ear canal which occurred between the experimental sessions. The distortion of the stimulus sound was negligible

A contraction of the middle ear muscles changes the acoustic impedance of the middle ear and upsets the balance of the 800 cps "measuring tone The resulting output signals from both ears were recorded simultaneously on a two-track tape recorder and later processed

The amplitude of the impedance change at the end of the stimulus tone was measured and expressed in per cent of maximal obtainable change The mean of the two values at each stimulus level was plotted as a function

of stimulus sound pressure (in dB re 0.0002 μb or in dB re the ipsilateral reflex threshold after recovery). An amplitude of 10 per cent of maximal impedance change was designated as threshold. In persons with normal reflexes, four stimulus-response curves were obtained at each stimulus frequency, two for ipsilateral and two for contralateral stimulation. Only two such curves could be made on the patients with unilateral Bell's palsy.

Four patients, aged 24–27 years (two males and two females) were selected from an investigated group of 40 patients with peripheral facial palsy. None of the selected subjects had suffered from any ear disease or any neurological disease previous to the palsy. Their pure tone thresholds were normal. No significant impedance change could be elicited from either side in the paralyzed ear except for a few cases in which high threshold impedance changes could be induced by ipsilateral stimulation of the "paralyzed ear". This change may be due to either a weak stapedius contraction or a contraction of the tensor tympani muscle. The muscle contraction causing this impedance change was regarded to be without significant effect on the sound transmission because the impedance change was small, and had a high threshold.

Measurements were performed during the acute state of stapedius paralysis and several times thereafter to 8 months after recovery. Recovery was regarded as complete when the stapedius reflex became equal on both sides. The influence of the stapedius reflex on the stimulus tone was determined as the change in intensity of the stimulus tone presented to the affected ear after recovery necessary to elicit an impedance change in the contralateral ear equal to that obtained during paralysis. Such comparisons were warranted since the reproducibility of the reflex measured with the acoustic impedance technique is high over long periods of time (Møller 1962). The impedance change was thus used as a relative measure of the cochlear excitation.

RESULTS

Figure 1 illustrates the change in the acoustic impedance in the contralateral ear in response to pure tone stimulation (500 cps, 1000 msec duration) of the ear on the affected side in a patient with peripheral facial palsy of short duration. Recordings obtained during paralysis are shown in the left column and those found after total recovery are depicted in the right column. When the magnetic tape recordings were processed the output was aligned with respect to amplitude. This alignment permitted the maximal impedance change obtained on the healthy side (with ipsilateral stimulation) to give the same deflection (100 per cent) during and after paralysis.

The amplitude of the reflex responses at the different stimulus intensities are smaller after the recovery and the time course of the response is characteristically changed (Fig. 1). The oscillations in the response (frequency about 5 cps) appear as a result of the amplitude regulation provided

muscle contraction on the sound transmission are from animal experiments (*Wiggers, 1937 Wever & Bray 1942 Wever & Vernon 1955* Simmons, 1959 Galambos & Rupert 1959 Møller 1965) In man most of these studies have been performed using psychoacoustic methods (Perlman, 1938 Jepsen 1955 Shapley 1954 Loeb & Riopelle 1960 Reger 1960 Ward 1961 Fletcher & Loeb 1962 Hansen 1965) In addition direct measurements on postmortem temporal bones have evaluated the effect on sound transmission by artificially applied forces to the middle ear structures (Neergaard *et al.*, 1963 Elpern *et al.*, 1965)

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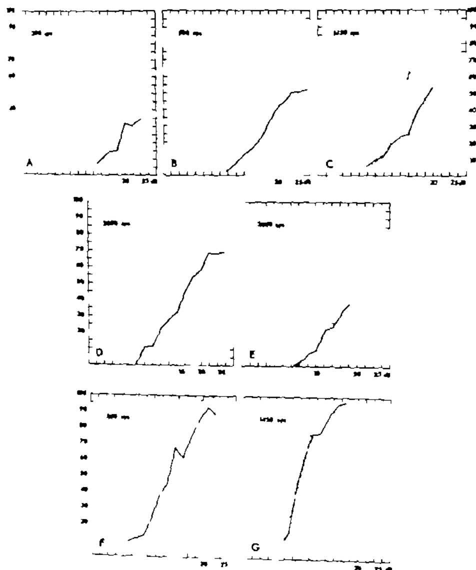


Fig. 2. Impedance change per cent of maximal obtainable as a function of sound level in dB re ipsilateral reflex threshold. The hatched line shows the contralateral reflex during ipsilateral stapedius paralysis and the solid line relates to the reflex after recovery. (Subject L. H. and I. D.)

an impedance change of a given amplitude after recovery than before. The magnitude of the shift is a direct measure of the attenuation provided by the stapedius reflex action. The shift is greatest at low frequencies (Fig. 2 A, B, F). At high frequencies (2000–3000 cps) the shift is very slight except in some cases at the highest intensities used (Fig. 2, D). As a rule the individual differences appeared to be greater at around 1600 cps than 1000 cps as indicated in Fig. 2 C and G.

The difference in shift of the stimulus-response curves between the two

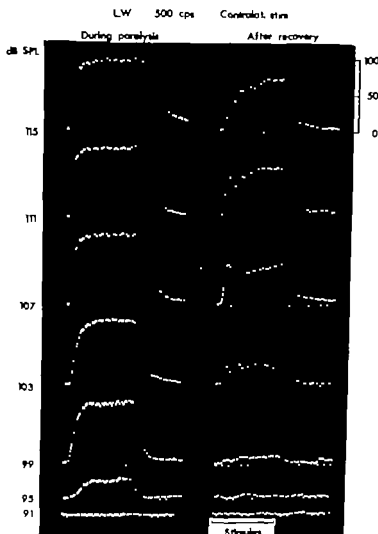


FIG. 1 Changes in acousti impedance in the contralateral ear at various stimulus intensities as a fun tion f tim llcited by a 500 cps ton (1000 m duration) f the affected ar during paralysi (*l ft lumn*) d ft complet reco ery (*right column*) Scale h ws relative impedan hang On subject (L. W)

by the reflex These fluctuations were generally more pronounced on the ipsilateral side

Figure 2 shows typical results from two patients In these graphs the amplitude of the impedance change measured at the termination of the stimulus and expressed in per cent of the maximal obtainable ipsilateral response is plotted as a function of the stimulus intensity The ordinate shows relative reflex response and the abscissa demonstrates the sound pressure (in dB above the ipsilateral stapedius reflex threshold in the affected ear after recovery) These curves depict the reflex response of the unaffected ear which was elicited by stimulation of the affected ear during stapedius paralysis (hatched line) and after recovery (solid line)

A shift to the right of the stimulus response curves after recovery of the stapedius function implies that a higher stimulus level is needed to obtain

mal (i.e. at the same intensity as the impedance change in the contralateral ear is maximal) After the normalization of the stapedius reflex the contralateral impedance change reaches a plateau which is lower than before (solid line in Fig. 2 B D) This means that the stapedius reflex prevents the excitation in the cochlea from increasing further to reach the same level as during palsy When the excitation in the cochlea is maximal the activation of the ipsilateral reflex will probably be close to its maximum. At sound pressures where the ipsilateral reflex activity (in the ear which had been affected) approaches its maximum (about 20 dB above its threshold) also the attenuation can be expected to be maximal However Fig 3 A illustrates that the rate of ascend of the attenuation increases at stimulus intensities around 20 dB re. threshold This increased growth rate is also seen in some curves in Fig 3 B even at lower intensities. At 500 cps a 1 dB increase in sound intensity in the ear canal is reduced 0 6 to 0 7 dB during the transmission through the middle ear when the stimulus strength is below 20 dB re. reflex threshold (Fig. 3 A) A corresponding increase in stimulus intensity will be reduced by nearly 1 dB if the stimulus intensity exceeds 20 dB re threshold. A certain change in the sound pressure in the ear canal will thus result with a very slight change in excitation of the cochlea if the sound pressure is higher than 20 dB above the ipsilateral threshold. In this case the stapedius reflex is a nearly perfect regulator which keeps the output of the middle ear independent of variations in the input Thus the amplification in the feed-back circuit must have increased.

DISCUSSION

The results of quantitative impedance measurements in subjects with unilateral Bell's palsy confirm the findings mad with other methods in both animal (see e g Galambos & Rupert, 1959) and in man (see e.g. Ward, 1961 Neergaard et al 1963) These reports generally indicate that a stapedius contraction decreases the middle ear's transmission mainly of low frequency sounds. It is found in this present study that a pure tone of 500 cps, with an intensity of about 20 dB (re. the ipsilateral stapedius reflex threshold) is attenuated 12–15 dB A tone of 1450 cps at an intensity of about 15 dB (re reflex threshold) is attenuated only 0–6 dB At higher frequencies (2000–3000 cp) the attenuation found was very slight except at th highest intensities used.

The attenuation of low frequ ncy sounds increased in direct proportion with the intensity of the stimulus which elicited the reflex up to a certain lev l (see Fig. 3) The rate of ascend of the attenuation increased at the highest intensities used The increased amplification in the feed-back circuit brings the ystem quite close to "perfect regulation" This implies that the excitation in the cochlea is quite constant and independent of considerable variations in sound pres ure in the ear canal. This is illustrated in Figs. 2 and 3 which indicate an almost perfect regulation between

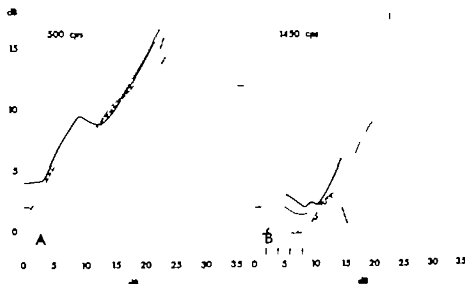


FIG. 3 Att nuation of a 500 cps (*left graph*) and a 1450 cps (*right graph*) pure tone in four subjects as a functi n f sound lev l in dB re ipsilateral reflex threshold. The ipsilateral reflex threshold (10% impedance chang) I at 500 cps respecti ely 93 (———) 95 (- - - -) 90 (- — —) and 96 ( ) dB SPL.

frequency ranges and the individual variations in the attenuation during different degrees of reflex activity is visualized in Fig 3 The graphs in this figure are obtained from pairs of stimulus response curves similar to those shown in Fig 2 and illustrates the results from measurements on 4 subjects at 500 cps and 1450 cps. The shift of the stimulus-response curves (in dB) is plotted as a function of stimulus strength (relative to the ipsilateral threshold of the affected stapedius reflex after recovery)

The curves to the left indicate that the decrease in transmission at 500 cps is proportional to the intensity of the "stimulus tone At 20 dB above threshold the attenuation is 12–15 dB The course of the curves showing the attenuation at 1450 cps is more varying and at 16 dB the attenuation ranges from 0 to 6 dB An extrapolation indicates that the curves approach origo for 500 cps This means that the change in acoustic impedance at 800 cps (measuring tone) has the same threshold as the decrease in the transmission of tones in the 500 cps range On the other hand, the attenua tion at higher frequencies (1450 cps, to the right) is insignificant below 5–10 dB re ipsilateral threshold for the impedance change at 800 cps Thus a greater activity of the stapedius muscle is required in order to influence the acoustic properties of the ear at 1450 cps than at the lower frequencies of 500 and 800 cps

The hatched curves in Fig 2 (A B F G) show that the impedance change in the contralateral ear reaches a plateau when the stimulus strength on the paralysed side attains a value 10–15 dB above the reflex threshold This asymptote may be due to mechanical properties of the contralateral (nonstimulated) middle ear and needs not imply that the out put from the ipsilateral middle ear or the excitation in the cochlea is maxi

reflex. The contralateral reflex activity can thus be expected to be less well correlated to the protective effect than the ipsilateral reflex activity This hypothesis has, however not been tested.

As indicated in Fig. 3 the individual variability in the attenuation of a 1450 cps pure tone is greater than of a 500 cps tone. In animal experiments it has been shown that tones of frequencies mainly below the resonance frequency of the middle ear are attenuated by the stapedius reflex (Møller 1965) Since the resonance frequency of the human middle ear is about 1000 cps the variability in attenuation of 1450 cps can partly be explained by the differencies in the natural frequency of the middle ear in the different subjects.

While the increase in stiffness of the middle ear affects mainly low frequencies, the "decoupling" of the cochlea (observed at very high inten sities) is less dependent on frequency (see Figs. 2 and 3) Such decoupling could explain the attenuation of high intensity tones well above the resonance frequency of the middle ear as observed by others (Chisman & Simon, 1961 Hansen 1965)

By comparing the stapedius reflex elicited from the ipsilateral and con tralateral side respectively it is possible in some cases, to find out if the sound transmission through the middle ear is "perfectly regulated or not. In almost all patients with facial paralysis, the maximal amplitude of the impedance change in the unaffected ear was the same when obtained by ipsilateral stimulation as by stimulation on the side of paralysis. On the other hand, after recovery the maximal amplitude of the impedance change was lower when elicited from the contralateral side than when evoked by ipsilateral stimulation. This decrease in maximum means that the intensity of the sound transmitted does not increase to the same level as when th stapedius muscle is paralyzed, even if the sound pressure in the ear canal is increased This difference in maximal impedance change f llowing ipsilateral and contralateral stimulation, is often seen in subjects with normal hearing and normal reflexes (Møller 1961 *b*) which thus indi cates that the transmission is "perfectly regulated In some cases, however n maximal level of the contralateral impedance change was not reached, w thin the range of timulus intensities used.

The vibration *pattern of the footplate at various degrees of stapedius* activity may be dependent of the construction of the "stapedio-vestibular" juncti n The ction of the stapedius reflex as a "perfect regulator" of sound transmis ion through the middle ea is in that case dependent on the characteristi s of this junction. In support of the observed variability in reflex properties (Møller 1961 *b* and this study) it can be mentioned that Engström (1948) ha shown that the tapedio-vestibular junction in man varies from a true joint to a syndesmosis.

From the preceding discus ion it i suggested that there are 3 objective criteria for an estimation of the static attenuative capacity of the stapediu refl x in normal subjects. These are (1) the threshold of the ipsilateral

300 and 2000 cps at the highest intensities At lower intensities the attenuation can be explained by an increased stiffness in the middle ear's sound conductive system At higher intensities (20–25 dB above reflex threshold) some additional factor must be responsible for this increased attenuation. One possible explanation can be derived when considering the effects of the stapedius action on the position of the footplate and the tension in the anular ligament When the stapedius muscle contracts, the stapes is moved posteriorly out of the oval window The position of the footplate is changed so that the tension in the anular ligament becomes more symmetrical than before Strong contractions may thus create the conditions for the rotational axis of the footplate to be moved centrally and away from its normal position at the footplate's edge This shift implies that a stapes movement is accompained by a *smaller effective displacement* of the cochlear fluid (Møller 1961 *a*) and this change in vibration mode of the footplate may act to partially "decouple" the cochlea from the middle ear

In experiments on the guinea pig Mundie (1963) has shown that at very high stimulus intensities the cochlea is "decoupled" from the middle ear in the presence of intact middle ear reflexes He suggests that the "decoupling" may depend on a disarticulation of the incudostapedial joint Such an explanation presupposes that the disarticulation is practically total However such separation was not observed even following strong electrical stimulation of the muscles in the cat (Møller 1967) It cannot be stated whether or not the nonlinearities observed in the present study (Fig 2 solid lines) are accompanied by production of overtones. Wever & Bray (1942) did not obtain an increased content of overtones except at artificial tensions in the stapedius muscle which were considerably above physiological values A nonlinearity in the middle ear peripheral to the stapes might be the cause of the 'perfect regulation' observed above 115 dB SPL (500 cps) *This is, however highly unlikely as Guinan & Peake (1967) failed to* find appreciable distortion in the middle ear below 140 dB SPL in the deeply anesthetized cat

Several parameters are of importance in determining the individual static attenuative effect of the stapedius reflex The reflex threshold shows great individual differences (Jepsen 1955 Møller 1962 Dallos, 1964) and is thus probably an essential cause to individual differences in the susceptibility to hearing damage by noise (cf Fig 3) However Loeb & Fletcher (1961) and Ward (1967) could find no more than a slight correlation between noise-induced temporary threshold shift and contralateral reflex activity The contralateral reflex activity is, however dependent on both the excitability of the reflex arc and the attenuative effect of the ipsilateral reflex The activity of the contralateral reflex is inversely related to the attenuation brought about by the stapedius reflex on the stimulated side The extreme case is illustrated in Fig 2 which shows that the contralateral reflex activity is much greater when a low frequency stimulus is applied to an ear with a paralysed stapedius than to an ear with a normal stapedius

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reflex activity (2) *the natural frequency of the middle ear* (3) the relationship between the ipsilateral and contralateral maximal impedance changes

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ZUSAMMENFASSUNG

An Patienten mit einseitiger peripherer kurzzeitiger Facialisparese wurde die Einwirkung des Stapediusreflexes auf die Schalleitung durch das Mittelohr untersucht Die Aktivität des Reflexes wurde dabei in beiden Ohren gleichzeitig als Änderung der akustischen Impedanz bei 800 Hz registriert. Als reflexauslösende Stimuli dienten ein Töne von 1 sek Dauer im Bereich von 300 bis 3000 Hz. Durch Vergleichsmessungen während des akuten Stadiums der Parese und nach dem vollständigen Verschwinden der Lähmungserscheinungen konnte die Einwirkung des Stapediusreflexes auf die Fortleitung dieser Stimuli durch das Mittelohr bestimmt werden Dabei wurde die Amplitude des gekreuzten Stapediusreflexes, d h der Ausschlag der Impedanzänderung, als relatives Mass der Cochleaerregung der affektierten Seite benutzt Aus den während und nach der Lähmung gemessenen Veränderungen in den Registrierungen des gekreuzten Reflexes konnte so die Grösse der Einwirkung des normalen Reflexes auf die Fortleitung des Tonstimulus durch das Mittelohr erhalten werden

Die durch den Reflex bewirkte Dämpfung war grösser für Frequenzen unterhalb der Resonanzfrequenz des Mittelohrs (ungefähr 1000 Hz) als oberhalb der Resonanzfrequenz Ein 500-Hz Tonstimulus von einer Stärke von 20 dB oberhalb der Reflexschwelle wurde um 12 bis 15 dB gedämpft während ein Ton von 1450 Hz von 16 dB oberhalb der Reflexschwelle nur um 0 bis 6 dB gedämpft wurde. Im besonderen konnte gezeigt werden dass für einen 500-Hz Ton von 115 dB SPL die Cochleaerregung nach Behebung der Lähmung ein niedrigeres Maximalniveau erreicht als während der Phase der Parese Diese Abnahme der maximalen Erregung legt den Gedanken nahe, dass der Stapediusreflex im Bereich seiner Maximalaktivität gleichsam als perfekter Regulator der Schallfortleitung durch das Mittelohr wirkt Möglicherweise kann diese Regulatorwirkung ihre Erklärung darin finden dass der Schwingungszustand des Stapes durch eine starke Stapediuskontraktion geändert wird und dadurch die Energieüberführung zur Schnecke vermindert wird

Die Oszillationen in der Amplitude der Impedanzänderung die bei Auslösung des Reflexes mit tieffrequenten Stimuli auftreten beruhen wie gezeigt werden konnte auf der Stapediusaktivität der stimulierten Seite.

Abschliessend wird erörtert, wieweit sich aus den Messungen die protektive Einwirkung des Stapediusreflexes an gesunden Personen beurteilen lässt In diesem Zusammenhange wird besonders betont, dass es wesentlich ist auch die Aktivität des ipsilateralen Reflexes aufzunehmen

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HEMANGIOMA OF THE TONGUE

A Case Report

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An abnormal lingual condition is reviewed from the standpoint of speech physiology, speech production, phonetic analysis, and surgery. The importance of an objective evaluation is discussed as well as the techniques utilized for the evaluation. The surgical results for this case are also reported.

Most pathological enlargements of the tongue in infancy and childhood are due either to hemangiomas, lymphangiomas or combinations of these two. These represent growths of blood or lymph vessels which are independent of normal circulatory channels.

Cavernous hemangioma (angioma racemosum) is a plexiform, ramifying angioma which has extended diffusely into the musculature of the tongue and has caused marked enlargement. The term, cirsoid, is sometimes applied to these angiomas and indicates the presence of multiple arteriovenous shunts within the substance of the angioma. In many instances, the child has a moderately enlarged tongue at birth which undergoes rapid and marked increase in size. Deformity of the mandible, erosion or decay of the teeth, and bleeding of the tongue will occur if treatment is not instituted. A surgical wedge resection is the preferred method of treatment. While radiation has been used in some instances, the dosage necessary to destroy these tumors has resulted in a poor functioning fibrotic tongue and the potential irradiation injury to the adjacent developing structures in the oral cavity of children precludes the use of radiation as a method of treatment.

The patient with an hemangioma of the tongue is not seen frequently in clinical situations dealing with anomalies of the oral mechanism. Chandra & Prakash (1965) have described, in the section on rare and obscure cases of the *British Journal of Surgery*, two unusual cases of extensive suppurative parenchymatous glossitis due to pseudomonas pyocyaneus and haemolytic streptococcus. In these cases enlargement of the tongue was

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Fig. 2. Frontal iew of the tongue fter the first surgical procedure

plete these tests without any difficulties. Cinefluorographic analysis of tongue movements showed that the dorsum of the tongue did not hump in an abnormal fashion during sustained phonation or during connected speech. Cinefluorographic films were also produced of the vertical and horizontal movements of the tongue and tape recordings were made of the patients speech.

Since the speech of such patients is likely to be affected, the speech pathologist should be called upon to evaluate the speech of the patient with an hemangioma of the tongue Evaluation procedures should utilize a standard articulation test as well as tests of lingual mobility which can be timed and compared with some standard, prior to and following surgery In the present case the articulation errors were recorded before and after surgery Thus it is necessary to study and record the lingual movements and lingual size in an objective manner such as from cinefluorographic analysis. The cinefluorographic technique was utilized with the present case These studies are important not only during the initial evaluation, but they will be extremely advantageous when re-evaluating the patient after urgery nd during the dditional follow-up procedures which will be con du ted. Changes in articulat ry proficiency as recorded on an articulation evalu tion, and or lingual-motor devi ti ns, noted during cinefluorographic analysis, m y serve as an indication f recurrence of a corrected condition. Thi can be useful in alerting the urgeon to changes that have taken place

ZUSAMMENFASSUNG

Es wird ine Überal ht gegeben über eine male Zungenbeschaffenheit vom Standpunkt der Sprechphysiologi Sprechprod ktion, phonetischen Analyse und



FIG. 1 A Hemangioma of th tongue Condition of th tongu before surgery

FIG 1 B View of the side of the tongu bef re surgery

present Luchsinger & Arnold (1965) note that pathological changes of the tongue structure can be acquired or be congenital and with the con genital alterations one rarely encounters what is truly called an enlarged tongue—macroglossia

The purpose of this study was to describe the pre- and post surgical speech characteristics of a patient who had an abnormal lingual condition

This case is presented because it is rare and a case like this is not often observed in the regular speech clinic This patient had a congenital large cavernous hemangioma of the lower lip tongue and floor of the mouth and right side of the palate When the child was first admitted for surgery at the age of six, her enlarged tongue protruded from her mouth past her chin as shown in Fig 1 A and 1 B The patient substituted the voiced (th) sound for the (s) consonant and the plosive consonants (p) (b) (g) and (k) were distorted In Fig 2 is shown a frontal view after successful lingual surgery This patient now has a mild malocclusion and still some difficulty articulating the (g) and (k) consonants, but her overall speech has shown a marked improvement She was given parts of a motor disability test (Westlake 1952) which could be timed pertaining to opening and closing the mouth and selective activity of the lips. The patient was able to com-



FIG. 2. Frontal view of the tongue after the first surgical procedure.

plete these tests without any difficulties. Cinefluorographic analysis of tongue movements showed that the dorsum of the tongue did not hump in an abnormal fashion during sustained phonation or during connected speech. Cinefluorographic films were also produced of the vertical and horizontal movements of the tongue and tape recordings were made of the patient's speech.

Since the speech of such patients is likely to be affected, the speech pathologist should be called upon to evaluate the speech of the patient with an hemangioma of the tongue. Evaluation procedures should utilize a standard articulation test as well as tests of lingual mobility which can be timed and compared with some standard prior to and following surgery. In the present case the articulation errors were recorded before and after surgery. Thus it is necessary to study and record the lingual movements and lingual size in an objective manner such as from cinefluorographic analysis. The cinefluorographic technique was utilized with the present case. These studies are important not only during the initial evaluation, but they will be extremely advantageous when re-evaluating the patient after surgery and during the additional follow-up procedures which will be conducted. Changes in articulatory proficiency as recorded on an articulation evaluation, and or lingual motor deviations, noted during cinefluorographic analysis, may serve as an indication of recurrence of a corrected condition. This can be useful in alerting the surgeon to changes that have taken place.

ZUSAMMENFASSUNG

Es wird eine Übersicht gegeben über eine anomale Zungenbeschaffenheit vom Standpunkt der Sprechphysiologie, Sprechproduktion, phonetischen Analyse und

Chirurgie. Die Bedeutung sowohl einer objektiven Auswertung als auch der dabei gebrauchten Techniken wird diskutiert. Die chirurgischen Resultate für diesen Fall werden ebenfalls mitgeteilt

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CARCINOMA IN PLEOMORPHIC ADENOMA OF THE PAROTID GLAND

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In a survey of 1678 tumours of the parotid gland, a histological reclassification resulted in 1302 of them (77.6%) being registered as tumours with the structures of a pleomorphic adenoma (mixed tumour). Altogether 1281 were classified as benign, and 21 (1.6%) as malignant. None of the tumours classified as benign was observed to show any form of malignancy, i.e. metastases or caused death of the patient. The histological findings in the 21 malignant tumours indicate the possibility of a new epithelial tumour with malignant growth properties developing within an already existing benign pleomorphic adenoma—a "malignification". The long clinical course before the diagnosis of malignancy, as well as the subsequent short survival time in the present series, lend support to the view of malignification of a primary benign tumour. On the basis of this study the authors suggest the term carcinoma in pleomorphic adenoma as being more adequate than "malignant mixed tumour". In comparison with other types of malignant tumours of the parotid gland—such as adenoid cystic, acinic cell, and mucoepidermoid carcinoma—the prognosis proved to be worst in carcinoma in pleomorphic adenoma.

The histological features of pleomorphic adenoma of the salivary glands (synonym mixed tumour) have been thoroughly described in recent years (Foote & Frazell 1954, Eneroth, 1964) and the tumour group is distinctly delineated nowadays, in view of a clear histological definition. Malignancy in pleomorphic adenoma is rare and exhibits a highly variable histological picture. This has led to difficulties in clearly defining histologically this type of tumour which we have chosen to denote as carcinoma in pleomorphic adenoma. The reason is the presence of a carcinomatous component of varying type such as adenoid cystic, mucoepidermoid, or anaplastic, in the otherwise benign pleomorphic adenoma (Moberger & Eneroth, 1968).

Pleomorphic adenoma is the commonest type of the comparatively rare tumours of the salivary glands.

Although pleomorphic adenoma is also found at other sites, such as lacrymal gland and skin, its most common localization is to major salivary glands, and especially the parotid gland. Thus, Rauch (1959) stated, on the basis of a review of several series, that 81% of all pleomorphic adenomas in the parotid gland, 8% the submandibular gland, and only 8% all other sites together.

Although pleomorphic adenoma has become increasingly distinctly delimited in recent years, there is still considerable disagreement regarding its malignancy This is evident for example, from the fact that the concept of *semi malignancy is so often applied to this type of tumour Certain histological* features (e.g high cellularity cylindromatous structures, and incomplete encapsulation) have, in fact for many years been considered to indicate potential malignancy (semi malignancy) Systematic studies of the *correlation between these criteria of semi malignancy and the clinical course* in large series (Eneroth 1964 1965 Eneroth & Hjertman, 1966) have, however shown that the histological criteria of semi malignancy are not associated with any clinical signs of malignancy and that the sole indicator of an unfavourable prognosis is infiltrative, destructive growth of the tumour

Some uncertainty nevertheless still exists about whether a pleomorphic adenoma without demonstrable infiltrative growth can unreservedly be denoted as a benign tumour Thus, a matter that has been difficult to evaluate from the point of view of malignancy is the presence of considerable cellular polymorphism in one of the components of a pleomorphic tumour without demonstrable infiltrative growth Moreover there is still great uncertainty with respect to whether such a focus of cellular polymorphism in an otherwise benign pleomorphic tumour is the morphological expression of a malignification or whether the pleomorphic tumour as a whole can possess malignant growth properties, while retaining its pleomorphic structure—i e., is a primary malignant tumour

The object of the present investigation was to analyze in a large series of pleomorphic adenomas with a long follow up period various criteria of malignancy

MATERIAL AND METHOD

The study is based on a histological and clinical survey of parotid tumours in 1678 patients, seen at Radiumhemmet Stockholm, from 1909 to 1958

A histological reclassification according to modern nomenclature (Eneroth, 1964) was made of all tumours. The prerequisites for a histological re-examination existed in all these 1678 cases, since slides and tissue blocks are archived at the Institute of Radiopathology Stockholm After histological re-examination of the 1678 tumours, pleomorphic adenoma structures were found in 1302 tumours—1281 pleomorphic adenomas and 21 carcinomas in pleomorphic adenoma During the lengthy follow up period, none of the 1281 patients with a tumour classified histologically as *pleomorphic* adenoma developed metastases, or died of the tumour disease

The 21 patients in the series with carcinoma in pleomorphic adenoma were operated on from 1923 to 1958, and all were traced up to 1964 This type of *tumour was present* in 14 men and 7 women The age of the patients at the onset of the tumour disease ranged from 19 to 80 years (mean total 43 1 men 42 3 women 44 8) The age at the first operation from which material for *histological examination was obtained* ranged from 20

to 82 years (mean total 52.1 men 49.4 women 53.9) The follow up period was counted from the first histological verification of the tumour Local recurrences, metastasis, survival time, survival rate, and other clinical features were studied in these 21 cases.

A rough estimate of the prognosis is obtained by calculation of the determinate survival rate. This implies that the survival rate is based on determinate groups, which do not include patients lost to follow-up, or those dying without signs of the tumour disease Since no patient in the present series was lost t follow-up, the determinate survival rate is based on the mortality in the tumour disease

Microscopical features

The safest way of recognizing a pleomorphic adenoma is to demonstrate a myxoid or a chondroid component, in addition to epithelial structures (Figs. 2, 3, and 7) In 14 of the 21 cases, either a myxoid or a chondroid component was demonstrable in 6 of them, both these types of component were present. In 7 of the 21 cases, neither a myxoid nor a chondroid component could be identified thus, these 7 tumours were purely fibroepithelial, but of a type recognizable as typical of pleomorphic adenoma. No tumour was so dominantly fibromatous and with pallisading of the nuclei as to simulate a neurinoma—a feature sometimes seen in pleomorphic adenoma.

Other mesenchymal tissue components (lipomatous, osteomatous) were present in only one of the tumours, which contained lipomatous structures.

The structure of the epithelial component of the 21 tumours was generally adenomatous (Figs. 3 and 4) or solid (Figs. 1 6, and 7)

Epidermoid differentiation was present in 4 tumours, although it was never f very high degree In 11 tum urs, fibroepithelial, more cellular areas were identified (Figs. 4 and 6) In 7 of them a cylindromatous structure was observed. In 8 tumours, more dark-celled, basalomatous structures were present, and in 4 of the 11 tumours a combination of both these pattern was found.

We hav pplied th term carcinoma in pleomorphic adenoma" only to cases i which infiltrative destructive growth could be demonstrated in *a t mour with structures typical of pleomorphic* adenoma However in 4 of the 21 cases, infiltrati e growth of the tum ur into urrounding tissue could n t be demon trated in the first pecimen a ailable for histological examin tion. In 2 f the 4 cases, thi can be explained by the first operative procedure bei g hiefly in the nature of a biopsy Consequently the specimen a ll bl did not permit evaluation of uch growth. Re-operation wa perf rmed within a few month of the first one the material then obtained allowed the ex stence of infiltrati e growth into urrounding tissue to be establ hed in b th cases. In the remaining 2 cases as well, in which infiltra ti growth wa bserved later a minor primary peration had been per formed, which m y hav resulted in infiltrative growth having been over looked at this operation



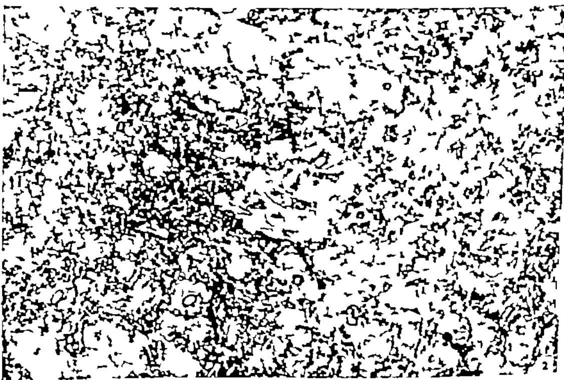


FIG 1 Carcin m n pleom rphi d m M ly solid, carci m lik t m H & E. 100

FIG. 2. Sam tum n Fig 1 Are with w ll-recog izabl fibro-myxo-epith lial tumo r tissu H & E. 100

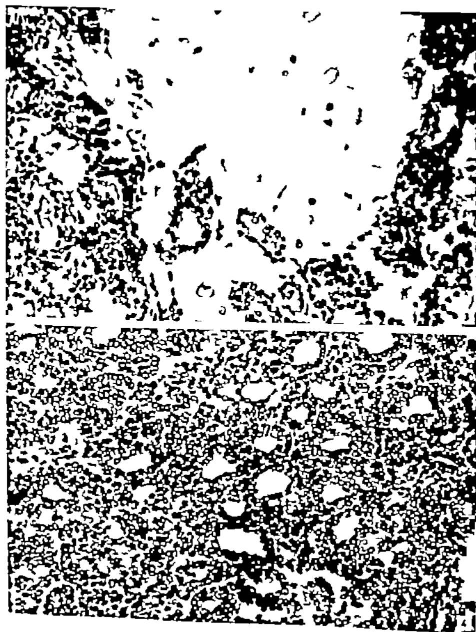


Fig. 3. Carcinoma in pleomorphic adenoma. Primary tumour with fibro-myxo-epithelial structure of benign appearance. No proof of malignancy found in operation specimen. V. Gieson. 200.

Fig. 4. Same tumour as in Fig. 3. More cellular but not highly polymorphous fibroepithelial tumour area of benign appearance. V. Gieson. 200.





Fig 5 Same pat t l Figs. 3 nd 4 Cervical lymph nod m t t l f mal ly solid carci oma type 1 yea fter first perati n. N pleom rph d ma struct re in metastatic tum ur tissu H & E. 100

Fig 6. Carcin ma in pleom rphic d noma Tum u cellular b t ot highl polymor phous, with a cylindrom t pattern. N proof f m lignancy in thi pecimen. V Gi son. × 100



Fig. 7. Another rea of the same pecimen 1 Fig. 6. The fibro-myxo-chondro-epitheli l pattern is evident. Van Gieson. 100.

In the specimens first examined histologically the cell picture was poly morphous in 12 cases. Although the polymorphism was generally moderate it was marked in one tumour Mitotic figures were seen in 11 cases, and in 6 of them they were numerous, i.e. it was easy to find at lea t one mitotic figure in most high-power fields. In 3 cases, peri- or intraneural growth w s demonstrated. In n case did we observe an exces ive lymphoid stroma reaction of the type seen in acinic cell carcinoma (Eneroth *et al* 1966) mucoepidermoid carcinoma (Jakobsson *et al* 1968) and to some extent in mucus-producing adenopapillary carcin ma (Blanck *et al*)

The hist logical structure of the tum ur type seems able to differ in the primary tum ur and in its recurrences. Thus, in 5 cases, it was n t possible t ident fy the pleomorphic denoma tructures in the last operative specimens. In 3 f them, th pattern w s th t f a solid carcinoma, and in 2 it w that of n immature mesenchymal tum ur

In 3 cases, meta tases were allabl for hist logical study In 2 of them, the met t si had the tructure of a s lid carcin ma (Fig) One patient had meta t ses in the skin of the scalp of aden id cystic carcin ma type Fig 8

Cl nical f tures

The nt rval between the onset of the tum ur disease nd operation with the fi st hi tologically examined specimen ranged from a few months to 41 years (me n 9.3 years) In 6 cases, the interval exceeded 20 years. In all but 2 cases, th time lapsing between the first sympt m of the tumour and



F o 8 S m patl t as in Fig 6 and 7 M tast l to the kl of the scalp with th appe ra c of an d ld cystl carcin ma H & E. x 260

demonstration of malignancy was practically the same as that between the onset and operation with the first histologically examined specimen. In these 2 cases, malignancy was not demonstrated until a recurrence 2 and 7 years, respectively after the primary operation The average interval between onset of the tumour disease and histological verification of malignancy—i e carcinoma in pleomorphic adenoma—was 9 5 years.

Few symptoms were noted Apart from the palpable swelling in the parotid region in all 21 cases, the only symptom was pain (recorded in 5 cases) and spontaneous paralysis of the facial nerve (3 cases)

The diameter of 3 tumours was less than 3 cm that of 4 from 3 to 5 cm, and in 6 cases it was more than 5 cm In the remaining 8 cases, the diameter was not stated

One tumour was first interpreted as a pharyngeal tumour and it was not until 22 years later that it was disclosed to be a parotid tumour with parapharyngeal growth Reliable data on the exact localization attachment, consistency and delimitation of the tumours were too few and uncertain to permit any detailed discussion

TREATMENT

Surgery

The operation at which the tumour was first histologically verified was generally conservative Thus, it consisted of excision in 14 cases, and of a minor procedure—mostly of biopsy type—in 4 Parotidectomy was per

formed primarily in only 3 patients. Secondarily a more major intervention was carried out in several of the cases in which the primary operation had been conservative

Radiation therapy

All patients had received radiation therapy It consisted of external irradiation and/or intracavitary radium therapy at operation.

External irradiati n was given by the short-distance telegamma techniques, using either telerad um units or ^{60}CO units with 6–7 cm between the radiation source and the skin (Walstam, 1965) Either one circular field 6 cm in diameter was used, or a combination of 2–4 such fields, 6–7 cm apart The estimated dose at 2 cm depth was generally of the order of 4000–5000 rads, given over 1–3 weeks. P eoperative irradiation only was given in 3 cases, and postoperative irradiation only with short-distance techniques, using either teleradium units or ^{60}CO units with 6–7 cm between the diation.

Intracavitary irradiation was given by applying one to four 50-mg radium sources enclosed in a metal container 10 mm in diameter for 3–12 hours. Thi type of therapy was applied in 6 cases In 2 of them, preoperative irradiation was given as well

Radiosensitivity

If a tumour that was easily palpable at the first examination was not definitely palpable 6 weeks after ending radiation therapy the radiosensitivity was considered to be high In n ne of the 4 cases given preoperative irradiation did the tum ur disappear clinically within 6 weeks of treat ment No definite conclusion about the radiosensitivity could be drawn in the group of 17 patient given postoperative irradiation.

CLINICAL FOLLOW-UP STUDY

The prognosi of the tumours was investigated by studies of the local recurrence metastasis, m rtality in th tumour disease survival time and survival rate particularly the determinate urvival rate

Local r urrence

A local recurrence fter the operation at which the tumour was first histologically erified occurred in 16 patients. However in 5 of them, it w n t a true local recurrence but rather a question of a tumour which, macroscopically had not been radically removed. Judging by the case re- p rts, the tumour wa inoperable in 4 of the 16 patients. Only one of the patients without a local recurrence died of the tumour disease, whereas the corresponding figure in those with local recurrence was 14 of 16

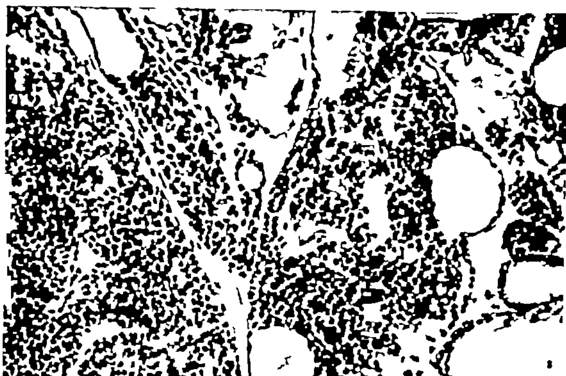


FIG. 8 Same patie t a in Figs 6 a d 7 M tast is t the skin of the scalp with the ppe rance of n d n id cystic rcinoma H & E. × 260

demonstration of malignancy was practically the same as that between the onset and operation with the first histologically examined specimen In these 2 cases, malignancy was not demonstrated until a recurrence 2 and 7 years, respectively after the primary operation The average interval between onset of the tumour disease and histological verification of malignancy—i e., carcinoma in pleomorphic adenoma—was 9.5 years.

Few symptoms were noted Apart from the palpable swelling in the parot id region in all 21 cases, the only symptom was pain (recorded in 5 cases) and spontaneous paralysis of the facial nerve (3 cases)

The diameter of 3 tumours was less than 3 cm that of 4 from 3 to 5 cm and in 6 cases it was more than 5 cm In the remaining 8 cases, the diameter was not stated

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Local re rrence

A local recurrence after the operation at which the tumour was first h tologically verified occurred in 10 patients. However in of them, it w s not a true local recurrence but rather a question of a tumour which, macroscopically had not been radically removed. Judging by the case reports, the tumour wa inoperable in 4 of the 16 patients. Only one of the 5 patient without local recurren e died of the tumour disease whereas the corresponding figure in those with a local recurrence wa 14 of 10

Metastases

Metastases appeared in 9 patients Regional lymph node metastases only were present in 4 patients, and distant metastases only in 4 whereas both regional lymph node and distant metastases were demonstrable in only one patient The distant metastases were localized to the lungs in 3 cases, to the skeleton (skull and upper arm) in one and to the skin of the scalp in the remaining case

Two patients with regional lymph node metastases died within 1 year of their appearance, and the other three after 3 7 and 9 years, respectively All 5 patients with distant metastases died within 2 years of their appearance

Survival time

Three of the 21 patients with a carcinoma in pleomorphic adenoma died of an intercurrent disease and 15 died of the tumour disease In these 15 patients, the survival time from onset of the tumour was less than 5 years in 2, 5–10 years in 6 11–20 years in 3, 21–30 years in 1 and more than 31 years in 3 patients The average survival time in these 15 cases was 15 1 years

In 19 of the 21 cases, the survival time after the diagnosis of malignancy was practically the same as that after the first histological examination of a specimen of the tumour In the remaining 2 cases, malignancy in the pleomorphic adenoma was diagnosed 2 and 7 years, respectively after the primary operation The survival time after the diagnosis of malignancy—i e., carcinoma in pleomorphic adenoma—was less than 5 years in 12 of the 15 patients, from 5 to 10 years in 2, and 13 years in the remaining patient

The survival time after the onset of spontaneous paralysis of the facial nerve was less than 2 years in all 3 cases

TABLE 1 *Carcinoma in pleomorphic adenoma*
5–20-year follow-up period

		Died		Determinate survival rate		
Observation period (yrs)	No. of patients	Tumour disease	No sign of tumour disease	No. of patients	No. of survivals	Survival ( )
5	21	11	—	21	10	48
10	19	13	—	19	6	32
15	1	13	1	16	3	19
20	11	9	2	0	0	0

Determine survival rate (D.S R)

The D.S R is a good criterion of the prognosis. All 21 patients were followed up for at least 5 years, 19 for at least 10 17 for at least 15 and 11 for at least 20 years The D S R. fell from 48% in the patients followed up for 5 years to 0% in the 20-year group (Table 1)

DISCUSSION

Tumours with the structures of pleomorphic adenoma are the commonest type of tumour involving the parotid gland. In the present series, they amounted to 1302 of 1678 histologically reclassified tumours—77.6%—an incidence somewhat higher than that of 64–72% given in other large series of histologically well-defined tumours of the parotid gland (Foote & Frazell, 1954, Beahrs *et al* 1960, Eneroth, 1964, Seifert, 1966).

In the present series, 21 of the 1302 tumours (1.6%) with pleomorphic adenoma structures were classified as malignant, i.e. carcinoma in pleomorphic adenoma. This incidence is in good agreement with the figures in large series reported by several authors (e.g. Beahrs *et al* 1960, Ackerman & del Regato, 1962, Eneroth, 1964) but is considerably lower than the figure of 10% given by Foote & Frazell (1954). This discrepancy in the incidence of malignancy in pleomorphic adenoma is to be ascribed to uncertainty regarding the criteria of malignancy and possibly also to certain difficulties in making a differential diagnosis between pleomorphic adenoma with cylindromatous structures and adenoid cystic carcinoma.

As far as the so-called histological criteria of semi-malignancy are concerned (e.g. high cellularity, cylindromatous structures, and incomplete encapsulation) the present study of 1281 pleomorphic adenomas showed that these criteria were not associated with any malignancy such as metastasis or death in the tumour disease. This supports the claim of one of us that it is not justified to base the concept of semi malignancy on these features (Eneroth, 1964).

According to Eneroth (1964) infiltrative destructive growth is the sole true histological criterion of malignancy in pleomorphic adenoma. The study of the present series supports this statement, in that the tumour disease was benign in all 1281 patients with a pleomorphic tumour lacking infiltrative growth, whereas 15 of the 21 patients with a tumour exhibiting infiltrative growth died of the tumour disease.

A small but nevertheless existing risk of using infiltrative growth as the only criterion of malignancy was demonstrated in the present series. It is true that such growth was present in all 21 cases of carcinoma in pleomorphic adenoma, but it was demonstrable in the first specimen obtained for histological examination in only 17 cases. In the other 4 the primary operation had presumably been too conservative so that there was insufficient marginal tissue around the actual tumour to evaluate this matter. Thus, a risk exists of overlooking the presence of infiltrative growth if there is an inadequate margin of tissue around the tumour. This implies that a pleomorphic adenoma with a focus of pronounced cellular polymorphism should not be regarded as a benign tumour merely because infiltrative growth cannot be demonstrated.

On the basis of the foregoing, we propose the following histological definition of the tumour type denoted as carcinoma in pleomorphic ade-

noma It is a tumour with the structure characteristic of pleomorphic adenoma and with histological signs of infiltrative growth into surrounding tissue A focus of pronounced cellular polymorphism should furthermore always be regarded as a suspicious finding

The aforegoing discussion mainly concerns the differentiation of carcinoma in pleomorphic adenoma from benign pleomorphic adenoma. The other important distinction is from other types of carcinoma i e the purely *epithelial malignant tumours* (acinic cell carcinoma adenoid cystic carcinoma mucoepidermoid carcinoma, mucus-producing adenopapillary carcinoma and solid poorly differentiated carcinoma) The presence of "mesenchymal" (e.g myxoid chondroid or fibroid) tumour tissue in a malignant *tumour also containing epithelial structures excludes it from these other* forms of carcinoma, and makes it necessary to assign it to the group of carcinoma in pleomorphic adenoma The greatest difficulty is encountered in those pleomorphic tumours which are purely fibroepithelial (lacking myxoid or chondroid structures) These have a characteristically luxurious and cellular fibroid component similar to that seen in the obviously pleomorphic adenomas. Here, the greatest difficulty in differential diagnosis is that from adenoid cystic carcinoma which has been discussed earlier by Thackray & Lucas (1960) and Blanck *et al* (1967)

A few isolated cases of pleomorphic adenoma, without histological signs of malignancy but with metastases of the same histological appearance as that of the primary tumour have been described in the literature (Foote & Frazell 1954) and have aroused great confusion and discussion We had a similar case in the present series, namely a patient in whom 14 years after operation of a primary tumour of the parotid gland (repeated local recurrences 5 years after the primary operation) two skin tumours appeared in the scalp Histological examination of both the recurrence in the parotid gland and of the skin tumours in the scalp showed *pleomorphic adenoma* structures without signs of malignancy The patient is still alive and asymptomatic—23 years after operation of the tumours in the scalp

In view of both the histological features and the clinical course the tumours of the scalp were regarded as primary tumours, and not as metastases to the parotid tumour It is, in fact, known that pleomorphic adenoma can occur primarily at many sites, such as the skin trachea, bronchi lachrymal sweat and mammary glands Consequently according to our histological criteria we have assigned this parotid tumour to the group of 1281 benign pleomorphic adenomas, this classification being supported by the clinical course We have evaluated the scalp tumours as multiple primary pleomorphic adenomas without signs of malignancy

Another question that has been much discussed and about which there is naturally great *uncertainty is whether a pleomorphic adenoma* is a primarily benign type of tumour which can become malignant or whether carcinoma in pleomorphic adenoma is a primarily malignant type of tumour

If primary malignancy were to exist in this type of tumour these tumours

should as a whole exhibit malignant pleomorphic structures moreover the structure of the metastases should also be pleomorphic. The focus of malig nant cells, often of adenocarcinomatous type seen in an otherwise benign pleomorphic adenoma structure argues against primary malignancy In addition, the metastases that were available for histological study did not, in any case, show any indications of pleomorphic adenoma structures, but had the structure of carcinomatous components of various kinds, such as solid carcinoma or adenoid cystic carcinoma. This does, in fact, argue in favour of development of a carcinomatous component within an otherwise benign pleomorphic adenoma.

This conclusion is also borne out by the clinical course In the majority of cases, this type of tumour had a long clinical course but once its malig nancy had been establi hed, the survival time was relatively short In our whole series of 1678 parotid tumours, the mean interval between the first evidence of tumour and histological verification ranged from 3.7 to 6.4 years in oth r types of malignant tumour such as adenoid cystic carcinoma, acinic cell carcinoma and mucoepidermoid carinoma In carcinoma in pleomorphic adenoma, this interval was much longer i.e., 0 years, and in 6 cases it exceeded 20 years. As far as the survival time after diagnosis of malignancy in the tumour is concerned, it was short—thus, 12 of the 15 patients who died of the tumour disease survived for less than 5 years.

The long preoperative duration of the tum ur as well as the short sur vival time after histological verification of carcinoma in pleomorphic adenoma, indicate that a malignification cannot be regarded as improbable In particular the 6 cases in which the interval between onset of the tumour and hi tological verification of a carcinoma in pleomorphic adenoma ex ceeded 20 years (it being 41 years in one case) suggest malignification in n initially benign tum ur Further evidence in favour of this iew is given by several the f ct rs, such a extremely rapid growth of tumour whose ize had p eviously been unchanged for a long time

The increasingly activ treatment of tum urs in recent years has led to the preoperativ duratio n of th tumour being greatly shortened This must imply that the ri k of pleomorphic adenoma being malignant i till lower th n that in the present series (1 6)

Thus, both th hi tological and the clinical study argue in favour of the dev lopment f a new tumour with malignant properties in an already existing benign pleomorphic adenoma. This i one of the reasons why we ha used the term carcinom in pleomorphic adenoma instead of "malig n nt mixed tum our which i probably th term still most used— car cin oma because in our experience it i in riably the epithelial component which ind cates malignancy of the tum ur Theoretically at any rate the exi tence f pleomorphic adenoma exhibiting malignancy of a sarcomat u type m ght be anticipated, although w have observed no uch tumour The term carcinom in pleomorphic denoma is nevertheles d fensible since these so-called mixed tumours are generally accepted nowadays as of purely

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A few isolated cases of pleomorphic adenoma, without histological signs of malignancy but with metastases of the same histological appearance as that of the primary tumour have been described in the literature (Foote & Frazell 1954) and have aroused great confusion and discussion We had a similar case in the present series, namely a patient in whom 14 years after operation of a primary tumour of the parotid gland (repeated local recurrences 5 years after the primary operation) two skin tumours appeared in the scalp Histological examination of both the recurrence in the parotid gland and of the skin tumours in the scalp showed pleomorphic adenoma structures without signs of malignancy The patient is still alive and asymptomatic—23 years after operation of the tumours in the scalp

In view of both the histological features and the clinical course the tumours of the scalp were regarded as primary tumours, and not as metastases to the parotid tumour It is, in fact known that pleomorphic adenoma can occur primarily at many sites, such as the skin trachea bronchi lachrymal sweat and mammary glands. Consequently according to our histological criteria, we have assigned this parotid tumour to the group of 1281 benign pleomorphic adenomas, this classification being supported by the clinical course We have evaluated the scalp tumours as multiple primary pleomorphic adenomas without signs of malignancy

Another question that has been much discussed and about which there is naturally great uncertainty is whether a pleomorphic adenoma is a primarily benign type of tumour which can become malignant, or whether carcinoma in pleomorphic adenoma is a primarily malignant type of tumour

If primary malignancy were to exist in this type of tumour these tumours

prognosis in adenoid cystic carcinoma and, to some extent, in acinic cell carcinoma a well as in carcinoma in pleomorphic adenoma, is poorer than that indicated by the 5-year follow up study In our series of mucoepider moid carcinoma, on the other hand, the D.S.R. was relatively unchanged from 5–20 years follow-up

It i evident that mucoepidermoid and acinic cell carcinoma have a considerably better prognosis than adenoid cystic carcinoma and carcinoma in pleomorphic adenoma The last mentioned has, in fact, the poorest prog nosis of all the malignant types of tumour compared in this series.

ZUSAMMENFASSUNG

Bei einer histologischen Nachuntersuchung von Tumoren in der Gl. parotl zeigte es si h, dass in 1302 v n 1678 Fällen ein Pleomorphic aden ma (Mischtumor) vorlag. 1281 Fälle wurden ls benigne und 21 Fälle (1,6%) als malign klassif ziert.

I kei em der Fälle bei denen der Tumor als benign kla sifiziert wurde kon te irgendwelche Form on Malignität wie Met stasen oder Tod in Tumor Erkra kung nachgewiesen werden. Die hist logischen Befunde bei den 21 malignen Tumoren prechen fü die Möglichkeit einer Entwicklung eines neuen epithelialen Tumors mit malignen Wachstumseigenschaften innerhalb es schon ex stierenden benignen Pleomorph c adenoma — einer Malignisierung. Sowohl der la g klinische Verlauf vor der M lignitätsdi gnose wi die dar uf folgende kurze Überlebenszeit in der vorliegenden Untersuchung bestätigen die Annahme einer Malignisierung ei es primä benignen Tumors. Auf Basis dieser Untersuchung schlagen die Verfa ser di Bezeich ung Karzinoma n Pleomorphic adenoma" als mehr ad quat l den Ausdruck „Mal gner Mischtumor" vor Bei ei em Vergleich m t nderen malignen Tumorarten in Cl. parotis — wi adenoid-zystisch ac n ll nd muko-epidermoid Karzin me — zeigte es si h, dass die Prognose bei Karz nomen in Pleomorph c ade oma m ungü stigsten wa

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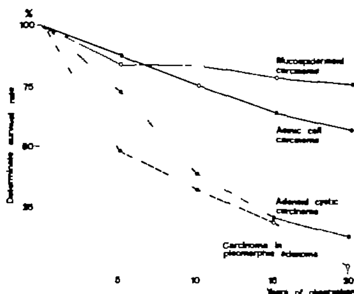


FIG. 9 Relati n between duration of observation and determinate survival rate (D.S.R.)

epithelial origin, despite the presence of tissue of a mesenchymal appear ance.

Carcinoma in pleomorphic adenoma is a rare malignant tumour of the parotid gland Thus, in the present series, it comprised 1.3% of all parotid tumours, and 7 0% of all malignant tumours involving this gland As a comparison it can be mentioned that adenoid cystic carcinoma accounted for 11 7% of all malignant parotid tumours in our series, acinic cell car cinoma for 12.3% and mucoepidermoid carcinoma for 21 1%

It is difficult to draw any conclusions about either the surgical or the radiological treatment since—during the long period in which the 21 patients were treated (1923–1958)—it was not uniform The high incidence of local recurrence may well have been due, in some measure, to an inade-quate surgical intervention With the current surgical technique and a more radical approach (parotidectomy and neck dissection) a lower inci-dence of recurrence could be expected and concurrently an improvement in the poor prognosis

Metastasis of carcinoma in pleomorphic adenoma was observed in 9 of the 21 cases (43%) In the present series of parotid tumours, the incidence of metastasis was as high in adenoid cystic carcinoma (43%) but much lower in acinic cell carcinoma (10%) and mucoepidermoid carcinoma (11%) The localization of the metastases indicates both haematogenic and lymphogenic spreading

The determinate survival rate (D S R) shows that the prognosis in car cinoma in pleomorphic adenoma is much poorer than that indicated by the 5 year follow up (Table 1) Thus, the D.S R fell from 48% 5 years after the first histological verification of the tumour to 0% after 20 years. In a comparison between the prognosis in various types of malignant parotid tumours in the present series it is apparent from Fig 9 that the long-term

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SOME SURFACE VIEWS OF THE INNER EAR BY LIGHT MICROSCOPY

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Investigation were performed by light microscope on the surface areas of the tympan l wall of the ductus cochlearis of the guinea pig, rabbit, cat d dog. Dissected pecimen of the cochlea after sil e reaction were used. Thi staining method wa very helpful in observing the structure w th fin high contrast.

When Huschke s teeth f th spiral limbs are iewed from above they ru from the modiolus toward the inner sulcus cell with man inter posed bridges between them. Th surface e tension f the interdental cells (superficial c lls f the spiral limbs) make radial mosaic pa e ment as wh le in th direction from the modiolus toward the inner sulcus ll with lightly i creasing surface area.

The free surface of the i ner sulcu ell becomes smaller toward the inner supporting cells.

The reticular membran maintain it compact structure in cases in which outer or inner ha r cells have fa led to d velop Th pattern of repair f the ret cular membrane wa shown.

At the border between Hensen s a d Claudius' cell a row of l ngitudi lly rranged ep thelial cells of on iderable ize w observed in the surface iew pec men The free surface f Hensen s cells f the first ow is lo gated outwards.

A long time l a p a sed ince Retziu (1884 described a great many sket hes f p n ramic view f the inner ear Kohonen (1965) and Eng trom *et al* 1966 hav adp ted phase contra t microscopy in the structural study f Corti org n, rep rting the precise urface views.

Although lectronmicrosc pic study provides fine precise structural find gs f th i ner ear it might be n t uitable for observing th struc t r w th wid a of Corti organ

In thi tu ly th urf ce observati n f the inner ear ha been carried ut fi lver reaction b light microscope and s me structural findings f C rti gan nd it adjacent area are reported.

MATERIAL AND METHOD

Cochl f the lbin guinea pig, c t albino rabbit and dog were studied The n mal wer nesthetized with admini tration of sodium pentobarbital (30 mg kg After decapitation the t mporal bones were removed and th

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R ei d April 30 1968

was dissected free in a suitable length from each coil of the cochlea and covered by cover glass with a drop of glycerin. A careful dissection was carried out under a binocular dissecting microscope with magnifications of ×10 to ×40

Some tissues were treated with hematoxylin-eosin after the above dissec tion

RESULTS

The tympanal wall of the cochlear duct runs spiral wise along the coch lea from the base to the apex. It consists of a thin center part, the basilar membrane which sustains the epithelium of Corti's organ, and of two thicker marginal parts, the spiral limbs and the spiral ligament which provide anchorage for the basilar membrane to the osseous spiral lamina and to the inner surface of the bony capsule

Superficial (interdental) cells of the spiral limbs

In the mid modiolar sections the spiral limbs appear as a triangular thickening sited on the osseous spiral lamina. It is homogennous or slightly filamentous and contains blood vessels and numerous cells near the sur face [illegible] thers deep down. The superficial cells are located in the interdental furrows, sited between Huschke's teeth These superficial cells of the spiral limbs run radially from the modi [illegible]lus toward the organ of Corti, ranging in close contact with one an[illegible]ther in orderly rows in the interdental furrows (Fig 2 a) Figure 2 b [illegible] a surface view of Huschke's teeth They make a complicated network near the area of insertion of Reissner's membrane and extend toward the inner spiral sulcu[illegible] with many bridges between them Electronmicroscopy (Iurato, 1962) showed that the filaments of Huschke's teeth run fr[illegible]m the base to the apex of each tooth. However the surface [illegible]iew gi[illegible]es an impression that they extend in a radial direction.

According t[illegible] th[illegible] electronmicroscopic investigations (Iurato, 1962 Naka [illegible] ma, 1960) these int[illegible]rdental cells are T-shaped, with the vertical portion [illegible] body within th[illegible] interdental furrow the horizontal portion expanded

F[illegible] 2 The surface [illegible]iew of the [illegible]piral l[illegible]mbs of the rabbit [illegible] cochlea. Interdental cell [illegible]perficial cell [illegible] the spiral limbs [illegible]rranged i[illegible] orderly rows, contact one [illegible] nother [illegible] [illegible] Hematox[illegible]lin-eosin. Middle turn [illegible] The surface [illegible]iew of the [illegible]piral limbs of [illegible] [illegible] [illegible] Radially ru[illegible] [illegible] Huschke's teeth [illegible] [illegible] with many bridges bet[illegible] [illegible] Silver stain Middle t[illegible]rn. (C) The [illegible]rface [illegible]iew of the superficial (inter den[illegible] [illegible] cell of [illegible] [illegible]piral limbs. Rabbit The horizontal cell processes construct [illegible] regu la[illegible] mosaic pa[illegible]ement [illegible] whole on the [illegible]piral limbs under the tectorial membr[illegible]ne Silver [illegible] Middle t[illegible]rn

F[illegible] 3 The [illegible]urface [illegible]iew of the i[illegible]ner [illegible]piral sulcu[illegible] cell[illegible] of the rabbit's cochlea The free surface of [illegible]ach inner [illegible]piral sulcu[illegible] cell i[illegible] becoming [illegible]maller tow[illegible]rd the org[illegible] of Corti [illegible] [illegible] Middle t[illegible]rn (b The surface [illegible]iew of the inner [illegible]pporti[illegible]g [illegible] of the rabbit [illegible] cochle[illegible] Silver stain, Middle turn. [illegible]) The surface [illegible]iew of the inner [illegible]pport ing cell[illegible] [illegible] the guinea pig' cochlea. Silver stain. Middle turn.

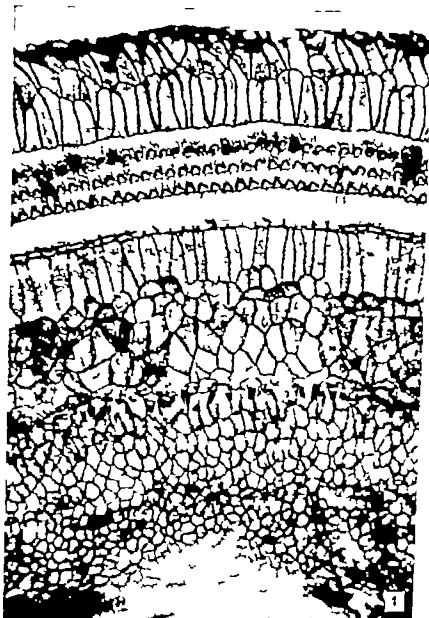


FIG. 1 Th general surf ce view of the cell structure n the ba ilar m mbrane f the guinea pig s cochlea. Middl turn

oval and round window were exposed through the bulla At the apex of the cochlea a small hole was opened by using dental instruments and a sharp needle After extraction of the stapes the round window membrane was opened and a 0.2% $AgNO_3$ solution at a temperature of 2–5 C was allowed to run through the cochlea from the round window to the apex with slight hydrostatic pressure in the same solution These materials were kept in the same $AgNO_3$ solution in a cold and dark chamber for 15 min then the cochleas were perfused with a 0.2% NaOH or a 0.2% KOH solution for a few seconds and immersed in a 10 formalin for 24 hours also in a cold and dark chamber The bony capsule of the cochlea was chopped away with the spiral ligament and the stria vascularis The tissue to be studied

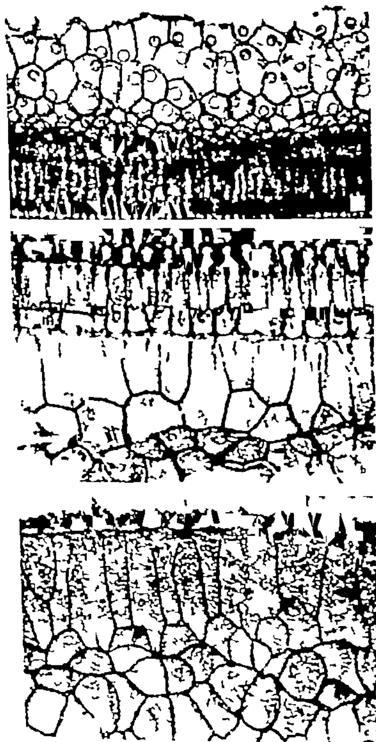


Fig 3

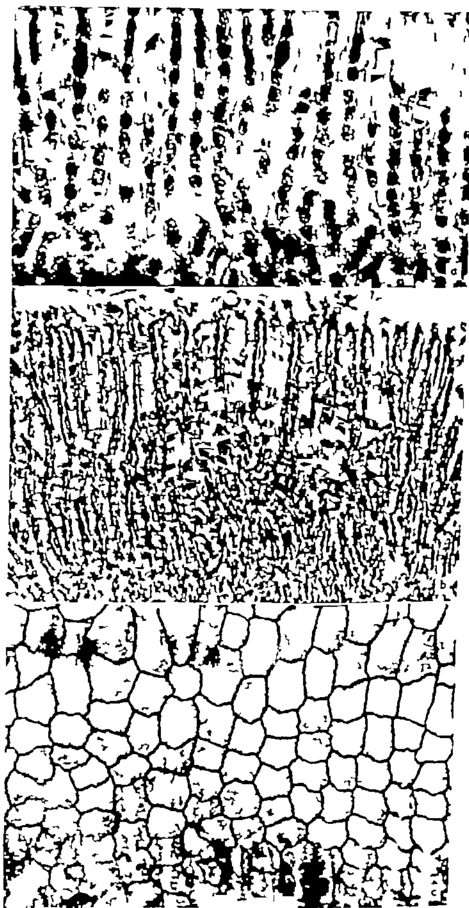


Fig. 2



Fig. 3

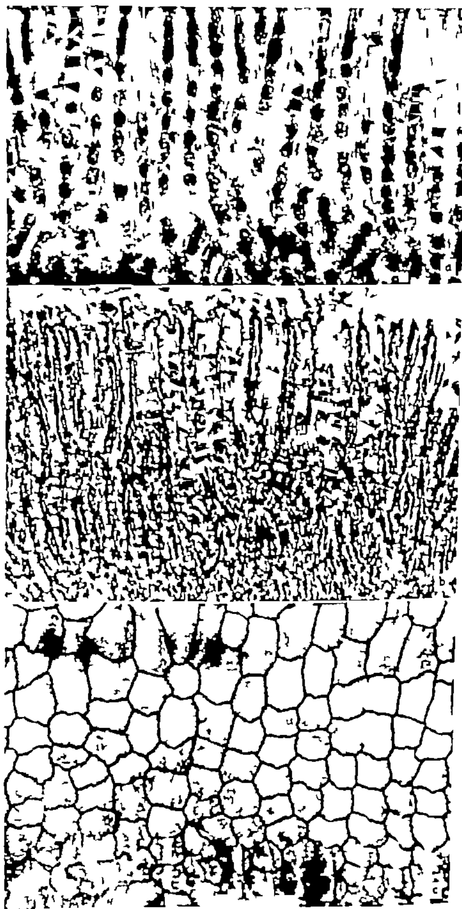


Fig. 3



Fig. 3

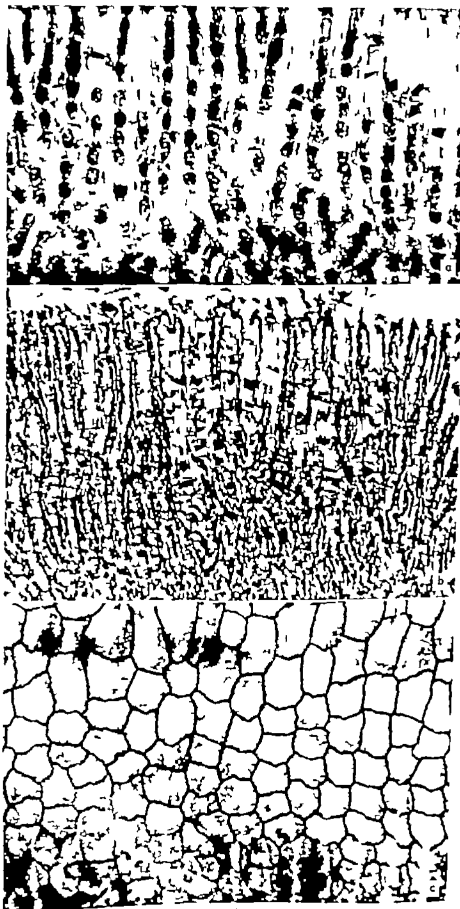


Fig. 2

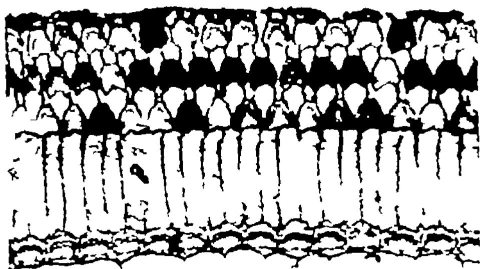


Fig. 4 The re[illegible] lar membrane of the cat's cochlea. The heads of the inner pillar cell [illegible] def ned Silver st [illegible] Middle t rn. (b) The reticular membrane [illegible] the same pig [illegible] cochlea. Sil er stain. Middle t rn.

above the free surface of Huschke s teeth The horizontal portion is a very thin process, widening out from the neck to cover the tip of Huschke s teeth Fig 2 c is a surface view of this horizontal thin process after removal of the inserted portion of the tectorial membrane

These flat processes make a regular radial arrangement all over the spiral limbs under the tectorial membrane They range in contact with each other with slightly increasing surface area toward the inner spiral sulcus where the last of these processes is in contact with the inner spiral sulcus cells This process has already been observed with light microscope (Ladowsky 1877 Held 1926 Retzius, 1884)

Inner spiral sulcus cells and inner supporting cells

From the inner spiral sulcus up to the pillar cells there are continous prismatic cells with increasing height toward the inner hair cells. The free *surface of the inner spiral sulcus cell (Fig 3 a) becomes smaller toward* the organ of Corti Between the inner sulcus cells and the inner hair cells, one or two inner supporting cells exist in the radial plane (Fig 3 b) In the guinea pig these two inner supporting cells are rarely seen (Fig 3 c) However in the rabbit these two inner supporting cells are not rare (Fig 3 b) The free surface of the inner supporting cell is larger than that of the inner sulcus cell In many cases, each inner supporting cell connects with the bodies of two inner hair cells.

The reticular membrane inner hair cells inner and outer pillar cells Deiters cells and outer hair cells

Figure 4 is the surface view of the reticular membrane of the cat (a part of the middle coils of the cochlea) A regular framework of the reticular lamina is indicated Especially the contour of the inner pillar cell head is clear between the row of inner hair cells and the first row of the outer hair cells With regard to the connections between the pillar cell heads and the reticular membrane the head of the inner pillar cells ends with a rectangular laminar process extending right up to and contacting the cuticle of the first row of outer hair cells From the head of the outer pillar cells a laminar process likewise proceeds outerward under the inner pillar lamina between the row of inner pillar cells and the first row of outer hair cells and it appears over the free surface of the reticular lamina, passing through the outer hair cells of the first row narrowing considerably and finally broadening at the end The tip is in contact with the second row of outer hair cell cuticle, while both the lateral sides are in contact with the phalanges of the first series of Deiters cells. In this respect the authors completely agree with the recent observation by Iurato (1961)

Figure 5 a and b are the surface views of the reticular membranes and adjacent areas of the guinea pig s cochlea Figure 5 a shows the surface

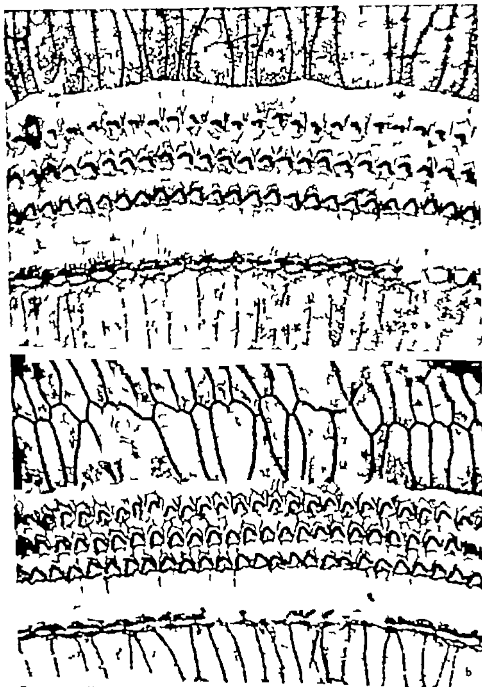


FIG. 5 The surface iew of the reticul membrane nd adjacent areas f the guinea pig' cochlea. The hair area on the hair cell cuticle is becoming maller in the tow rd the outermost row of the hair cells. Upper turn. S l stain. (b) The su face iew of the reticular membrane and adjacent areas of the guinea pig' cochlea. The bov mentioned characteristic is not so conspicuous as in the upper turn. Lower turn. Silver stain.

view of Corti s organ on a part of the upper coils The hair area of the hair cell cuticle where auditory hairs are planted is clearly visible and this hair area distinctely decreased in size toward the outer most row of the outer hair cells This characteristic feature is more conspicuous in the upper coils than in the lower coils (Fig 5 a) For detailed observations of auditory hairs, electronmicroscopy is indispensable and these details are found in the recent study by Kimura (1966) in which he corroborated that the hairs on the hair cell of the apical coil are taller than those on the hair cell of the basal one, but the number of hairs on each sensory cell is fewer

Figure 6 a is the dissected surface view of Corti s organ of a part of the middle coils of the rabbit s cochlea Certain deviations from the generally strict geometric pattern can be found In general there are three rows of outer and one row of inner hair cells in the tested animals. A few super numerary outer hair cells are often found in the third row and now and then four rows of outer hair cells can be observed for short distances

These supernumerary outer hair cells are not rare in the tested animals as a whole With regard to the inner hair cells these extra cells were not found in this study However according to Retzius (1884) and Engstrom *et al* (1966) these supernumerary inner hair cells may be found in some other species except the guinea pig

On the other hand irregularities of pattern of another type can be observed in which occasional hair cells are missing that is, have failed to develop (Fig 6 b 6 c) The important fact is that even if hair cells are missing or have failed to develop the reticular membrane maintains its own compact structure

As is obvious from Fig 6 b the defect of the outer hair cell of the third row is repaired by the two neighbouring hypertrophied Deiters cell phalanges of the second row The defect of the outer hair cells of the first and the second row are repaired by the two neighbouring hypertrophied outer pillar cell lamina

Figure 6 c shows two successive missings inner hair cells of the rabbit s cochlea In this case neighbouring inner pillar cell heads and the inner supporting cell become hypertrophied, replacing the defect of the reticular membrane The prismatic inner supporting cells which locate between the two missing inner hair cells show no evident alterations in this specimen

Hensen s and Cladius cells (Fig 7 a , b 7 c)

Hensen s cells are very high hexagonal prisms in shape with round nucleus and large fatty inclusions within the cytoplasm In the apical coils, Hensen s cells locate further from the modiolus The free surface which is raised like a dome-shape projecting into the endolymph shows irregular variabilities in size As a rule the free surface of Hensen s cells of the first row is elongated in the radial direction (Fig 7 a) Hensen s cells in the guinea pig s cochlea are least in number in the tested species of animals. In

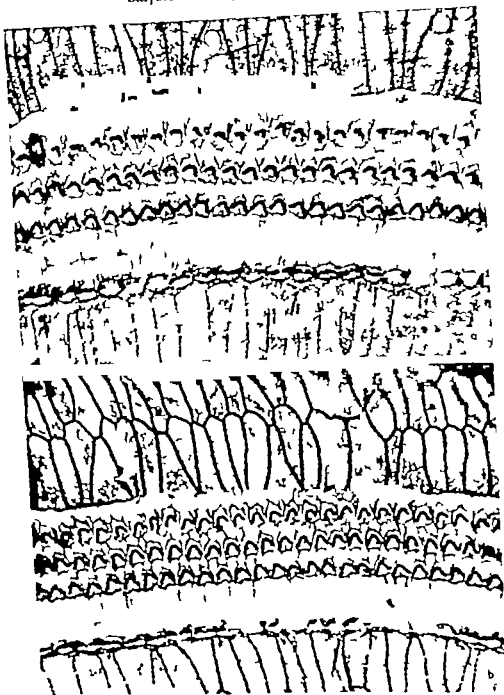


Fig. 3. The surface view of the reticular membrane and adjacent areas of the guinea pig cochlea. The hair rows on the hair cell cuticle is becoming smaller in size toward the outermost row of the hair cells. Upper turn. Silver stain. (b) The surface view of the reticular membrane and adjacent areas of the guinea pig cochlea. The above mentioned characteristic is not so conspicuous as in the upper turn. Lower turn. Silver stain.

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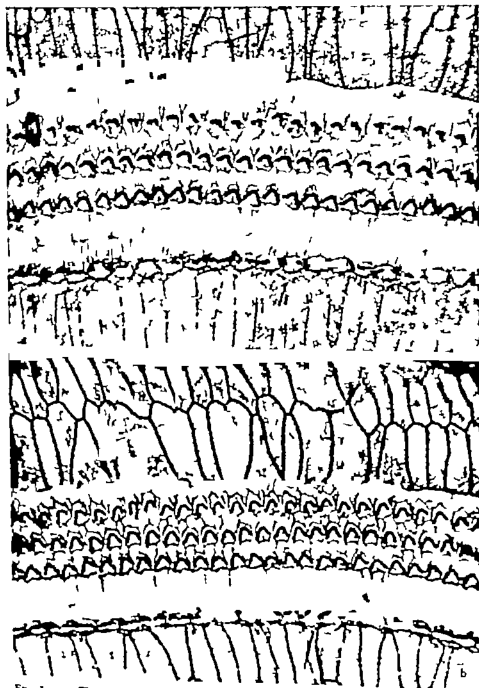


Fig. 3. The surface iew of the reticula membrane ad adjacent rea f the guinea pig's cochlea. The hair rea the hai cell cuticle is becomi g smaller in size tow rd the outermost row of the hair cells. Upper t rn. Silver tain. (b) The sur face view f the reticular membrane and adjacent reas of the guinea pig' cochlea. The bov mentioned characteristic is not so conspicuous in the pper t rn. Lower turn. Sil er t in.

the guinea pig there are 3–5 rows and in the rabbit, cat and dog 5–10 rows. Electronmicroscopy (Iurato 1962) revealed extremely regular hexagonal prisms of Cladius cells in the cross section They become shorter in height toward the outer spiral sulcus The surface view (Fig 7 c) shows that the free surface of each Claudius cell which is raised to the endolymph varies one another in size some are very small and others very large. At the border between Claudius and Hensen s cells a row of spirally arranged cells is clearly visible (Fig 7 c)

COMMENT

The superficial cells of the spiral limbs

The superficial cells of the spiral limbs are epithelial cells ranged in close contact with one another in orderly rows toward the inner spiral sul cus in the interdental *furrows* They are T *shaped* with the horizontal portion, which expanded over the spiral limbs, showing a radial mosaic pavement as a whole This horizontal expansion is covered with the tectorial membrane.

Iurato (1961) observed in this portion more numerous pedunclate vesicles in the young rat than in the adult one He suggested that the horizontal portion of the superficial cell of the spiral limbs expells a material into the tectorial membrane Voldrick (1967) found some signs of *secretory* activity on the superficial cells Embryological observations will furnish enough knowledges with regard to the relationship between tectorial mem brane and the superficial cells of the spiral limbs

The reticular membrane

The reticular membrane is composed of the heads of inner supporting cells, inner and outer pillar cells, phalanges of Deiters cells and the cuti cles of inner and outer hair cells. These components are tightly organized into a frame and the tunnel of Corti the space of Nuel and the other spaces within the organ of Corti are completely separated from the scala media

According to Iurato (1962) the reticular membrane is composed of an intracellular cementitious substance The fluid interchange between the endolymph and the fluid in the spaces within Corti s organ through the reticular lamina appears to be unlikely although one part of the hair cell top is free from cuticular plate (Kimura *et al.*, 1964)

Fig 6. (a) The framew rk f th reticul m mbra f the rabbit cochlea. Extra numerary cells are seen h re nd there Middl turn S l er stai (b) The reticul membrane of th rabbit cochlea Co g ital l of th ut h l cells l repaired with neighbouring supporting cells. *Middl turn. Si tai ( ) Th reticul r m m* brane f the rabbit's cochlea Co g ital loss of th two l h l cell is isible. This defect is repaired with two hypertrophied i pilla cell h ds. Middle t rn Sil er stain.



Fig. 6

Tasaki *et al* (1954) and Davis (1954) concluded from their elaborate electrophysiological studies that the endolymphatic space must be bounded by the reticular lamina not by the basilar membrane Our present study showed that even if hair cells are missing or have failed to develop occasionally the reticular lamina maintains its compactness which leaves no likeliness of free communication between endolymphatic space and the lymphatic spaces within the organ of Corti through the reticular lamina This suggests that some membrane system which separates the lymphatic *spaces of Corti s organ from the endolymphatic space is indispensable for* the transmission of nerve impulses

Hairs of the sensory cell

The hairs of each outer sensory cell are arranged in a W form the base of which faces toward the bony wall According to Kimura (1966) and Kimura *et al* (1964) the number of parallel rows of hairs forming the W varies in different species, and three rows are found in the cat and the guinea pig The hairs in the peripheral rows of the W are taller than those of the inner rows The hairs at the base of the W are longer toward the hair cells of the third row The hairs of the apical coil are taller than those of the basal coil but the number of hairs of each hair cell is fewer toward the apex These electronmicroscopic observations are completely in accordance with the present light microscopic views. The functional significance of these morphological differences in the outer sensory cell of each coil is not clear

On the other hand the hairs of the inner hair cell are more coarse and fewer than those of the outer hair cell and no significant difference is observed in different coils

Hensen s cells

Hensen s cells contact the endolymph with the greatest free surface among Corti s organ and these free surfaces have many microvilli toward the endolymph They extend fan wise toward the endolymph Fatty inclusions, vesicles and electronmicroscopically observed boundary canaliculi between the two neighbouring cells (Nakayama 1960 Iurato 1961) are conspicuous in Hensen s cells From these observations Nakayama (1960) believed that Hensen s cells provide hair cells with nutriment by absorbing it from the endolymph through their absorptive function Engstrom & Wersäll (1953) discussed the possible importance of the microvilli of Hensen s cells for resorption of endolymph

FIG. 7 ( ) The surface f Hensen cell in th d g cochl r the retikul m mbrane Hensen cell *of the first row* how l g ted f rm Middl t rn. Silver stain. (b) Th surf ce view of H sen cell in the rabbit cochlea Middl t rn Sil r stain (c) The surf ce view of H s d Cladi cell n th cat cochlea A row of spirally arranged lls int rpose between Hensen nd Cl di s cell (*arrowed*)

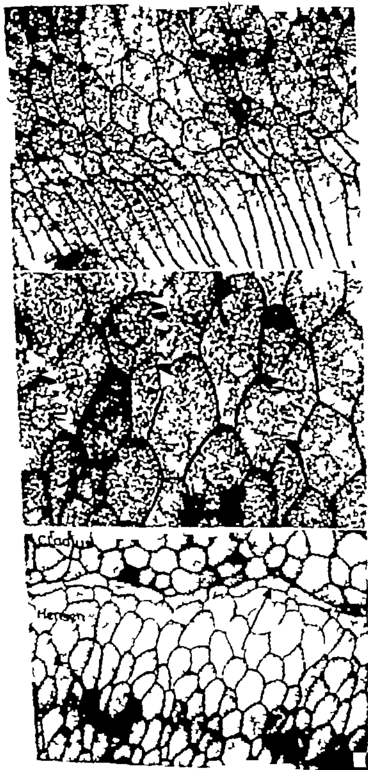


Fig. 7

De Vries (1949) freezing the cochlea with liquid nitrogen and Hilding (1952) and Tonndorf *et al* (1962) using intravital staining methods, believed that the tip of the tectorial membrane was attached to Hensen s cells in adult guinea pigs However the electronmicroscopic study by Kimura (1960) failed to demonstrate this connection in adult species, although its attachment to the outer edge of the reticular lamina is definitely observed in developmental phases of the organ of Corti At any rate, Hensen s cells may play a supporting roll to the organ of Corti and they also appear to have some other functions The fact that the free surface of Hensen s cells of the first row is elongated in the radial direction suggests that they support the organ of Corti mainly against the mechanical force which works toward the bony wall side At the same time this structure may favourably be related with the longitudinal bending of the basilar membrane during sound transmission (Békésy 1953)

ACKNOWLEDGMENT

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ZUSAMMENFASSUNG

Die häutigen Präparate der tympanalen Wand des Ductus cochlearis wurden nach einer Silberreaktion lichtmikroskopisch beim Meerschweinchen Kaninchen Hund und bei der Katze untersucht Diese Silberreaktion ist zweckmässig für eine mikroskopische Untersuchung mit deutlichem Kontrast.

Die häutigen Präparate der Huschkeschen Zähnchen des Limbus spiralis zeigen dass sie vom Modiolus bis zu den inneren Sulcuszellen radiär mit vielen Zwischenästen verlaufen Die freie Oberfläche der Zellen des Limbus spiralis ist zu den inneren Sulcuszellen hin immer grossflächiger

Die freie Oberfläche der inneren Sulcuszellen wird im Gegenteil immer kleiner zu den inneren Stützzellen

Die Retikularmembran behält ihre eigene Kompaktheit wenn auch einige äussere oder innere Haarzellen fehlen Und die reparierten Membranen wurden gezeigt

Zwischen den Hensenschen Zellen und den Claudiusschen Zellen fanden sich die in einer Reihe radiär angeordneten Zellen auf der Endolymphseite Die freie Oberfläche der Hensenschen Zellen von der ersten Reihe verlängert sich nach lateral

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Bei zwei Patienten konnte er keine Erklärung für dieses Phänomen geben. Auf Grund einer genaueren Auswertung dieser Fälle ist seiner Meinung nach die inverse Reaktion das Zeichen eines Prozesses in der Pauke, wodurch das runde Fenster blockiert wird, während die Mobilität des Stapes unverändert bleibt.

Gemäss unserer Erfahrungen tritt die inverse Reaktion beim Gellé-Versuch mit Luftleitung gar nicht so selten auf. Während unserer Untersuchungen, die wir mit einem fixfrequenten Impedanz Messgerät der Firma „Madsen" durchgeführt haben, konnten wir 15 Fälle beobachten.

Die Ursachen der Hörveränderung bei dem Gellé-Versuch sollen wir in den Impedanzveränderungen des Mittel- und Innenohres suchen. Bloch (1894) und Brühl (1898) waren die ersten, die den Gellé-Effekt mit der Impedanzveränderung erklärt haben. Der im Gehörgang erzeugte positive Druck spannt das Trommelfell und die Gehörknöchelchenkette an, damit wird die Steifheit erhöht, diese bedeutet auch Impedanzerhöhung, wodurch die Tonleitung verschlechtert wird. Die Minderung der Stapesbeweglichkeit hindert auch die Bewegungen der Perilymphe, dadurch steigert sich deren Impedanz. Gleiches geschieht, wenn man den Druck im Gehörgang mindert, jedoch wird in dem Fall das Trommelfell von dem grösseren Druck von der Pauke her nach aussen gewölbt. Der Erfolg ist auch in diesem Fall die Einschränkung der Beweglichkeit, also die Steigerung der Impedanz.

Bei dem mit Luftleitung durchgeführten Gellé-Versuch werden die Schwingungen durch die Trommelfell-Gehörknöchelchenkette in die Schnecke geleitet. Eben deswegen hat die Impedanzveränderung dieser Kette einen wichtigen Einfluss auf die Tonleitung. Die durch die Druckveränderung im Gehörgang verursachte Impedanzsteigerung verändert die Intensität des Tones schon, bevor er den Stapes erreicht hat. Dies ist die Ursache, warum sich die Lautheit eines Tones beim Gellé-Versuch im Falle einer Stapesfixation verändert und in jedem anderen Fall, wenn die Schwingungen auf diesem Weg zum Labyrinth gelangen können. Im entgegengesetzten Fall, wenn man den Ton mit Luftleitung vorgibt, kommt eigentlich das Hören durch Knochenleitung zustande. In dem Sinne können wir also über Luftleitung nicht sprechen.

Die Ursache der inversen Reaktionen muss man in den Faktoren suchen, die die Impedanz des Mittelohres beeinflussen. (Die Impedanzveränderung des Innenohres hängt nur davon ab.)

Einer der Faktoren, der die Impedanz des Mittelohres beeinflusst, ist der in der Pauke herrschende Druck. Die Voraussetzung der optimalen Tonleitung, also des besten Gehörs, ist, dass der Druck auf beiden Seiten des Trommelfells gleich ist. Ist dies gegeben, so ist die schwingungsleitende Fähigkeit der Trommelfell-Gehörknöchelchenkette optimal, ihre Impedanz minimal. Wenn der Druck in der Pauke von dem Luftdruck unserer Umgebung abweicht, verschlechtert sich das Gehör. Wird bei solch einem Fall der Druck im Gehörgang so geändert, dass er mit dem in der Pauke über

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ÜBER DIE AUSWERTUNG DER INVERSEN REAKTIONEN BEI GELLÉ VERSUCHEN MIT LUFTLEITUNG

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Die Ursache der bei dem Gellé-Versuch auftretenden inversen Reaktionen ist noch nicht völlig geklärt. Der Verfasser ist auf Grund der beobachteten 15 Fälle der Meinung, dass die Ursache der inversen Reaktionen in der Impedanzänderung der Trommelfell-Gehörknöchelchenkette zu suchen ist. Auf Grund seiner Beobachtungen teilt er die gesamten Fälle in 2 Gruppen. In der einen Gruppe finden wir inverse Reaktionen nur bei negativem Gehörgangsdruck. Bei positivem Druck ist der Versuch gesetzmässig. In diesen Fällen kommen in der Pauke steife Verwachsungen vor. Bei der zweiten Gruppe ist die Reaktion bei positivem sowie bei negativem Druck invers. Die Ursache hierfür finden wir in den zu lockeren Verbindungen der Trommelfell-Gehörknöchelchenkette oder bei ungenügendem Gespanntsein des Trommelfelles. Von den inversen Reaktionen, die wir bei dem Gellé-Versuch mit Luftleitung beobachteten, können wir auf den Paukenzustand rückschliessen.

In der Funktionsdiagnostik des Schalleitungsapparates nimmt der Gellé-Versuch einen vordringlichen Platz ein. Bei korrekter technischer Ausführung erbringt er wahrscheinlich den zuverlässigsten Beweis für oder gegen eine Stapesfixation. Die Untersuchung durchgeführt mit Luftleitung hat eine geringere Bedeutung. Man bekommt nämlich auch in dem Fall bei Stapesfixation *eine regelrechte positive Reaktion, da auf* Minderung oder Steigerung des Druckes im Gehörgang der untersuchte Ton leiser wird. Ausnahmsweise gibt es solche Fälle, wo im Gegensatz zur Regel bei Druckänderung *die Lautheit zunimmt. Dieses Phänomen können wir als* »inverse Reaktion« bezeichnen.

Gellé und Bloch (1894) haben schon in einigen Fällen inverse Reaktion beobachtet, aber sie fanden keine Erklärung dafür. Ullmann (1965) berichtet über einen Fall, wo bei Druckminderung Hörverbesserung auftrat, was er mit Ankylose der Gehörknöchelchenkette erklärt hat. Asherson (1952) führte in einem ähnlichen Fall auch eine Operation durch, aber der Operationsbefund war negativ, deswegen hat er angenommen, dass es sich um einen Muskelspasmus handelt. Weiterhin berichtet Thullen (1954) über vier Fälle, wo auf Drucksteigerung eine Hörverbesserung, jedoch auf Druckminderung eine Hörverschlechterung auftrat. Bei zwei von diesen Patienten *fand er je einen retromaxillären Tumor, der in die Pauke eingewachsen war.*

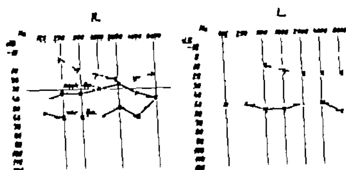


Abb. 2.

stützen. Ein solches Phänomen konnten wir bei sechs Patienten registrieren, bei denen der Trommelfellbefund und das Audiogramm auf eine Vernarbung in der Pauke folgern lassen.

Ein charakteristischer Fall war V J eine 32jährige Patientin. — Angeblich hat sich ihr Gehör in den letzten sechs Jahren verschlechtert. An Ohrenlaufen kann sie sich nicht erinnern, wurde jedoch ohne Erfolg mit Kurzwelle und der Politzermethode behandelt. Die Trommelfelle sind vernarbt. Ihr Audiogramm zeigt die Abb 2. Bei der Impedanzmessung haben wir normalen Paukendruck (entsprechend dem Luftdruck der Umgebung) gemessen. Bei dem Gellé-Versuch mit Luftleitung hat sich das Gehör wenn wir den Druck im Gehörgang gesteigert haben, verschlechtert. Bei Minderung des Druckes unte –50 mmWS verbesserte sich das Gehör Am 12.4 1967 führten wir die Tympanotomie durch die Schleimhaut des Promontoriums war erdickt, und der vordere Stapesschenkel mit dem Promontorium lamillär erwachsen. Der Steigbügel war fixiert Stapedektomie und Interposition wurden durchgeführt Nach der Operation hat sich das Geh r verbessert, wie wir es auf dem Audiogramm sehen können.

Diese Erscheinung können wir wieder mit der Impedanzveränderung erklären In diesen Fällen nehmen wir — wie Thullen — eine Vernarbung an, welche die Beweglichkeit der Gehörknöchelchen hindert Unsere Theorie wurd uch durch die Operation bewiesen. Die straffen Verwachsungen werden von dem Eindringen des Trommelfelles verursacht durch den Gehörgang überdruck, noch meh angespannt Dadurch verschlechtert sich die Schalleitung, der Ton wird leiser Bei negativem Druck aber bewegt ich das Trommelfell nach ussen, die Steifheit der straffen Gehörknöchelhenkette gibt nach, w s Impedanzminderung und damit bessere Schalleitung und Hörverbesserung bedeutet

Wir haben auch solche Fälle de inversen Reaktion beobachten können, wo bei gleichem Druck im Tympanon und im Gehörgang das Gehör am schlechtesten war Wenn wir im Geh rgang Unterdruck oder Überdruck erzeugen, wird das Geh r besser Das Resultat des Gellé-Versuches mit Luftl itung ist lso bei dieser Gruppe dem Gesetzmässigen entgegengesetzt

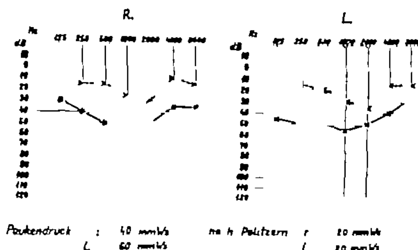


Abb. 1

einstimmt, bessert sich das Gehör. Dementsprechend wird sich die Lautheit des Tones während des Gellé-Versuchs mit Luftleitung zum Beispiel bei negativem Druck in dem Tympanon solange steigern — wenn wir den Druck im Gehörgang mindern — bis der Druck auf beiden Seiten des Trommelfelles ausgeglichen wird.

B. B. 43jährige Patientin bemerkt seit mehreren Jahren Schwerhörigkeit. An Ohrenlaufen kann sie sich nicht erinnern. Sie wurde mehrfach nach der Methode von Politzer ohne wesentlichen Erfolg behandelt. Bei der Untersuchung sind die Trommelfelle reizlos, matt, jedoch nicht eingezogen. Den audiologischen Befund zeigt die Abb. 1. Mit dem Impedanzmessgerät haben wir rechts −40, links −60 mmWS Druck in der Pauke festgestellt. Bei dem Gellé-Versuch mit Luftleitung berichtete die Patientin bei Steigerung des *Gehörgangsdruckes über leiseren, bei Minderung des Druckes über lauteren* Ton. Die Patientin gab den Ton rechts bei −40 mmWS, links bei −60 mmWS am lautesten an. Nach der Politzermethode haben wir die Untersuchung wiederholt, aber das Gehör hat sich nicht wesentlich geändert. Der Druck war jetzt beiderseits +20 mmWS. Bei wiederholtem Gellé-Versuch so bei Steigerung wie bei Minderung des Gehörgangsdruckes, empfand die Patientin leiseren Ton.

In manchen Fällen also kann man die inverse Reaktion mit der Druckveränderung in der Pauke erklären. Es ist aber keine echte, sondern nur eine pseudo-inverse Reaktion, die darauf hinweist, dass man bei der Auswertung der Untersuchung auch die Druckverhältnisse im Mittelohr in Betracht ziehen muss.

Bei der Mehrzahl unserer Patienten konnten wir ein echte inverse Reaktion beobachten. Bei einer Gruppe dieser Kranken hat sich das Gehör während positiven Gehörgangsdruckes verschlechtert, bei negativem verbessert. Dieses Phänomen erklärt Thullen mit der Verwachsung und Steifheit des Schalleitungsapparates, was auch unsere Untersuchungen unter-

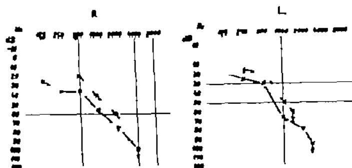


Abb. 4

Man darf aber die Funktion des M tensor tympani nicht ausser acht lassen. Unter physiologischen Umständen hat er wahrscheinlich die ent sprechende Steifheit des Trommelfells zu sichern. In bestimmten Fällen kann er aber seine Aufgabe nicht erfüllen, wie bei den obenerwähnten vier Patienten, wo die Vernarbung diese Ursache war Eine zweite Ursache kann z. B die Ermüdung des Muskels sein Nur mit dieser Tatsache können wir die zwei Fälle der obengenannten Gruppe erklären wo wir bei gesundem Trommelfell und negativer Anamnese hinsichtlich des Paukenzustandes während intensiven Lärms arbeitenden Patienten (der eine hat ausgesprochenen Lärmschaden aufgewiesen) inverse Reaktion gemessen haben

K. J ein 60jähriger Patient, arbeitete 12 Jahre lang in einem Lärmbetrieb, und zwar im Turbinensaal eines Kraftwerkes. Erst in den letzten Jahren bemerkte er eine Schwerhörigkeit Ein Ohrenleiden ist nicht bekannt. Trommelfelle reizlos. Sein Audiogramm zeigt die Abb 4 Die Impedanzmes ung stellte beiderseits normalen Paukendruck fest Impedanzwerte im Trommelfellniveau gemessen rechts 4 E, links 3 E. Bei dem Gellé-Versuch mit Luftleitung empfand der Patient auf Drucksteigerung oder Minderung die Verstärkung des Tones. Das Minimum der Lautheit kann beiderseits bei Druck 0 mmWS im Gehörgang registriert werden

Unsere Hypothese unterstützt dies, da wir in dieser Gruppe ausserordentlich kleine Impedanzwerte gemessen haben. (Normalerweise ist der Durchschnittswert 7,5 E, bei diesen Patienten war er 4,3 E.) Dieser niedrige Wert zeigt uns, dass der Ton von dem Trommelfell kaum zurückschallt, jedoch geht er für das Innenohr verloren — er verstreut sich wahrscheinlich in der Pauke

Mit diesen Untersuchungen wollten wir einerseits mit einigen Angaben dazu beitragen dass man die in ersen Reaktionen, die bei dem Gellé-Versuch noch nicht genügend geklärt sind besser versteht. Andererseits dienen un diese Angaben al Beweis, dass der mit Luftleitung durchgeführte Gellé-Versuch bei Tympanosklerose wertvolle Daten über den Paukenzustand erkennen lässt

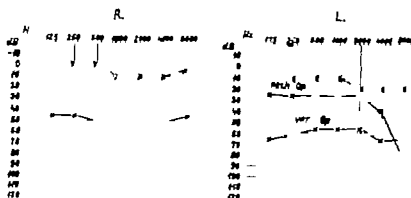


Abb. 3

Diese Reaktion haben wir bei sieben Patienten beobachtet Vier von diesen sieben Kranken zeigten beiderseits drei nur einseitig die inverse Reaktion Bei letzteren ergab die Untersuchung auf der anderen Seite normale Reaktion

Als Beispiel folgender Fall M G eine 36jährige Patientin bemerkt eine Horverschlechterung seit 6–8 Jahren Ohrenlaufen ist nicht bekannt Vor 3 Jahren wurde eine Stapesmobilisation mit vorübergehendem Erfolg wegen der Schwerhorigkeit durchgeführt Am 12 4 1966 wurde das Ohr reoperiert und eine Interposition durchgeführt welche eine anhaltende Hörverbesserung erreicht hat (Abb 3)

Ohrbefund rechts das Trommelfell ist matt vernarbt und atrophisch Links matt, reizlos

Das Gehör zeigt das Audiogramm auf der Abb 3

Impedanzmessung (13 12 1966) ergab links normalen Paukendruck In dem Trommelfellniveau gemessene Impedanzwerte rechts 3,5 E links 5 E. *(Gemessen mit dem Fixfrequenz Apparat nach Madsen)*

Bei dem Gellé-Versuch mit Luftleitung wurde rechts der Ton bei Überdruck sowie bei Unterdruck stärker Links auf der operierten Seite fanden wir regelrechte Reaktion

Die Erklärung für diese Erscheinung muss man wieder in dem Zustand der Trommelfell-Gehörknöchelchenkette suchen Gegenuber der vorher erwahnten Gruppe nehmen wir hier eine zu lockere Gelenkverbindung der Gehörknöchelchen an Wenn diese Verbindungen lockerer als normal sind wirken sie ebenso ungunstig auf die Schalleitung wie die zu steifen Über ahnliche Erfahrungen berichtet auch Beickert Er beobachtete bei lockeren Verbindungen die nach Interposition enstanden dass wahrend des Überdruckes nach der Politzermethode das Gehör vorübergehend besser wurde Wahrscheinlich spielten bei unseren Fällen ähnliche Ursachen eine Rolle da wir bei vier von den sieben Patienten auf dem Trommelfell atrophische Perforationsnarben fanden Ein so vernarbtes Trommelfell kann die Tonschwingungen nur dann aktiv übernehmen wenn es von einer Seite wie ein Segel angespannt wird.

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TYMPANIC MEMBRANE

Part II *Pars Flaccida*

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Submicroscopic morphological details of the pars flaccida (Shrapnell's membrane) of the cat squirrel monkey rabbit and sheep were studied Three layers were distinctly recognized outer epidermal, middle lamina propria and inner mucous. The epidermis was composed of three to four layers of keratinizing squamous cells, and the inner mucous layer was formed by a single-cell layer of simple squamous or cuboidal cells. These cells could accommodate cilia or secretory granules. The middle lamina propria was composed of loose connective tissue containing fibroblasts, nerve fibers and capillaries. The regularly arranged collagenous fibers which were present in pars tensa were not found Abundant elastic fibers were found in this layer intermixed with collagenous fibers. The thickness of Shrapnell's membrane in the materials used was considerably greater than that of pars tensa

Shrapnell (1832) first described the pars flaccida of the mammalian tympanic membrane He observed that this area in the goat, bulged when pressure was increased in the middle ear He then described this portion of the tympanic membrane as being more elastic than pars tensa and anatomically different and named it pars flaccida He described this portion of the membrane as having irregular fibers in place of the radiating fibers found in pars tensa.

Shrapnell's membrane was described by Kessel (1872) as a "very thin layer of cutis and of the mucous membrane of the membrana tympani. The cutis contains, in addition, the vessels and nerves, undulating bands of connective tissue." Marx (1935) also described lamina propria (Propriaschicht) as a distinct layer in the pars flaccida.

However Nishiyama (1937) stated in his tympanic membrane study that pars flaccida lacked a lamina propria The absence of a middle fibrous layer in Shrapnell's membrane has been well accepted, and it has generally been described that this part of the membrane was solely composed of an

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SUMMARY

The reason for the inverse reaction observed during Gellé tests with air conduction is not clear In connection with 15 cases of inverse reaction the author supposes the inverse reactions to be due to the impedance changes in the middle ear In the light of his observations he divides the cases into two groups In a number of cases inverse reaction is found only at a negative pressure in the auditory canal At a positive pressure the test gives a normal result In such cases there is a rigidity of the middle ear system In the other group the reaction is inverse both at positive and negative pressures. The reason for this can be found either in the too-loose connections of the ossicular chain or in the abnormal looseness of the tympanic membrane Thus the inverse reactions during Gellé tests with air conduction allow conclusions to be drawn about the state of the middle ear cavity

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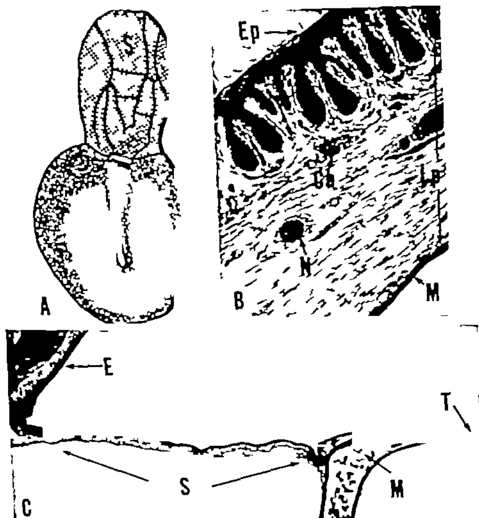


FIG. 1 (*A*) The rtist conception f the dissected tympanic membrane of the sheep, viewed from inside out. Neck of the malleu is severed. *S*, Shrapnell' membrane (*B*) Phase contrast micrograph of the heep pars flaccida. *Ep* epidermis; *Lp* lamina propria, *Ca*, capillary N nerv fiber *M* mucous layer (*C*) Arrows are demarcating Shrapnell' membrane (*S*) of the sheep. *T* pars t nsa *M* malleus; *E*, xternal canal skin.

Microscopic Observation

Squirrel m nkey

The thicknes of pars flaccida wa two to three times greater than that f pars tensa. The pars flaccida was a continuation of the cutis of the exter nal canal In a few instances, ceruminu u gland were observed near the border f the extern l canal. Myelinated nerve bundles and abundant capillaries were observed frequently in thi area (Fig. 2 A B and C)

outer epidermal layer and an inner mucous layer (Keller 1930 Eggston & Wolff 1947 Watkyn Thomas, 1953 Mawson 1963 Bloom & Fawcett, 1964 Lurie 1966) The morphological description of this layer is frequently misleading due to an unclear conception of lamina propria.

The purpose of this article is to demonstrate the existence of and clarify the conception of lamina propria in Shrapnell s membrane of various ani mals

METHOD

Ten to twenty tympanic membranes were obtained from four types of adult animals of both sexes cats, squirrel monkeys, rabbits and sheep The animals were decapitated and the middle ears were removed from the tem poral bone and immediately fixed in cold phosphate buffered osmium tetrox ide All of the other preparations of the specimens for light microscope and ultrastructural study were carried out in the same fashion as described in the previous articles (Lim *et al* 1967 Lim 1968)

Shrapnell s membrane was correctly oriented before embedding *in toto* The embedded specimens were cut in small pieces with a jeweler s saw and then remounted for thick sections varying from one to three microns Thin sections were cut by a LKB ultratome and double stained for electron micro-scopic examination The RCA EMU 2 and the RCA EMU 3 electron micro-scopes were used for ultrastructural observation utilizing magnifications ranging from × 900 to × 30 000

Gross Anatomy

Squirrel monkey

The shape of the pars flaccida of the squirrel monkey was triangular similar to that of the human and much smaller in proportion to the pars tensa

Cat

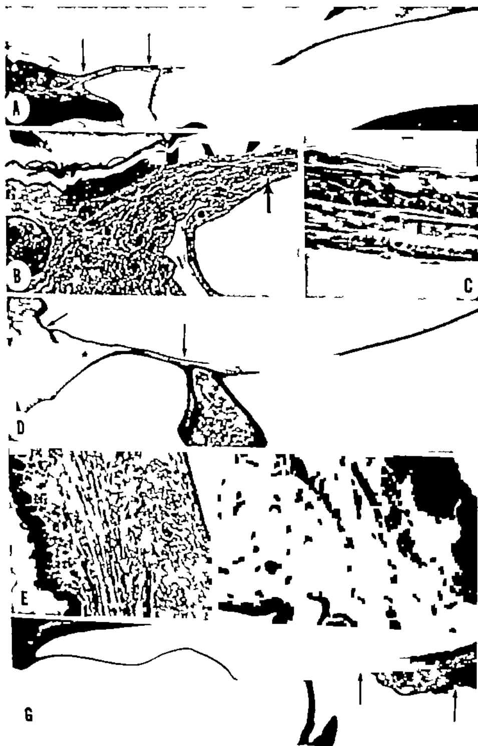
The pars flaccida of this animal was also triangular in shape The size of this portion of the membrane was proportionally a little larger than that of the squirrel monkey

Rabbit

The pars flaccida of the tympanic membrane of this animal was half of an ellipse and about one-fourth the size of pars tensa

Sheep

The pars flaccida of the sheep was the largest among the animals studied, approximately one-half the size of pars tensa and its shape was elliptical (Fig 1 *A*)


A
B
C
D
E
G

Cat

The pars flaccida was very thick and resembled an inverted triangle with its broad base attached to the bony portion of the external canal and its pointed portion continued to pars tensa Well arranged collagenous fibrous layers were lacking in this portion and the middle lamina propria was composed solely of loose connective tissue. Epidermal and mucous layers continued from pars tensa however the epidermis showed an interdigitating basal lamina The mucosal layer is basically a single-cell layer of mucosal epithelium but in a few instances pseudostratified epithelium with ciliated cells was observed (Fig 2 *D* and *E*)

Rabbit

The thickness of pars flaccida was 20–30 times greater than that of pars tensa This portion of the membrane was a continuation of the external canal cutis which contained abundant capillaries. The lamina propria was well-developed and consisted of irregular fibers. The mucous layer was infolded and continued to the middle ear mucosa (Fig 2 *F* and *G*)

Sheep

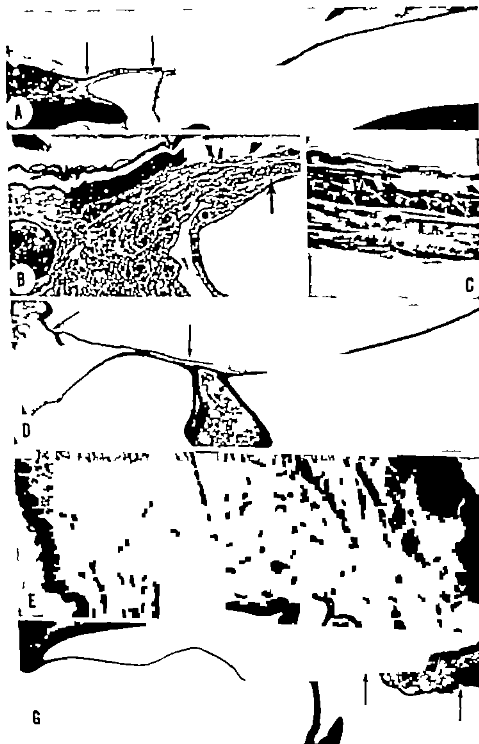
The thickness of pars flaccida was about 10–20 times that of pars tensa. The epidermis again was thicker than that of pars tensa and the basal layer occasionally showed a palisade appearance. The lamina propria was composed of loose connective tissue, abundant capillaries and nerve fibers. The lower portion of pars flaccida, which bordered pars tensa, contained a portion of a well arranged collagenous bundle layer which diffused into the lamina propria of pars flaccida. The cellular elements were very rich in this layer (Fig 1 *B* and *C*)

Electron Microscopic Observations of the Pars Flaccida

Epidermis

The morphological findings of the examination of the epidermis of the cat and the squirrel monkey were identical with that of pars tensa The rabbit and sheep have essentially the same layers as the cat and monkey

FIG. 2 (*A*) Squirrel m nk y' tympani m mbran w th arrows i dicating Shrap ll membrane (*B*) Phase ntrast micrograph of the pars flacc da f th squirrel monkey Arrow indicates ins rti n f fibro bu dl from pars t (*C*) Phase co trast micrograph of the pars t nsa f th squirrel monk y From th top, pid rmis, oute radi t nd inner circular fibrou lay rs, and mucou l yer re hown (*D*) Tympanic membrane f the cat with arrows indicating Shrap ll m mbra (*E*) Phase contra t micrograph of the cat Viewed from l ft to right: pid rmis, l min propria, and m cous lay r (*F*) Phase ontrast micrograph of th pars flaccida f th rabbit. Viewed from the right t left: epidermis, lamina propria and mucou l yer (*G*) Tympa ic membrane f th rabbit with rrows indicati g Shrap ll membra The arrows are located in th middle ear space


A
B
C
D
E
G

stratum corneum stratum granulosum and stratum Malphighi (*Fig* 3) However indentation of the basement membrane was more pronounced in the rabbit and sheep Keratohyalin granules in the granular layer were observed in all of the animals examined Tonofilaments were sparce in the cytoplasm of the epidermal cells of the rabbit and sheep Occasionally abundant ovoid membrane-coating granules (MCG) or Odland bodies were found in stratum granulosum (Fig 4 *B*) The epidermal cells of these animals contained many glycogen particles in the cytoplasm (Fig 3) Intercellular spaces in the Malphigian layer were wider in the rabbit and sheep (*Figs.* 3 and 4 *A*) than in the other animals In the basal layer hemidesmosomes were well developed in all of the animals, and nerve endings penetrated *into the epidermis as they did in pars tensa* Synaptic structures between nerve endings and epidermal squamous cells were not evident Mitochondria were small *and either round or elliptical Occasionally light* cells were found in between squamous epithelial cells, and they seemed to contain small vesicles and abundant mitochondria, thus resembling Merkel cells or tactile cells (Fig 6 *A*)

Lamina propria

This layer in all the animals was composed of numerous fibroblasts, collagen fibers and elastic fibers, with occasional myelinated and unmyelinated nerve fibers and capillaries (Figs 5 and 6 *B*) It was rather loose in texture and the spaces between the cellular and fibrillar components were filled with amorphous ground substances (Fig 7 *A*) Compact fibrillar *bundles—radial and circular fibers—were missing completely However* near the junction with pars tensa some finer fibrillar bundles emerged into the loose connective tissue of the pars flaccida (Fig 2 *B*) The fibroblasts in this layer had very long, slender cell processes with a spindle-shaped cellular body containing a round or an oval nucleus (Fig 7 *A*) There was no clear-cut morphological distinction between the subepidermal and submucosal connective tissue layers except for the presence of many capillaries, nerve fibers and wandering cells with fewer elastic fibers

Unmyelinated nerve fibers found in this layer were accumulated mostly near the subepidermal region and to *a lesser* degree *near the submucosal* region (Fig 8 *A*) They contained neurogranules and neurovesicles with an *occasional local* dilatation along their long axes (Fig 8 *B*) Schwann cell axon units (fundamental nerve units) were commonly found among the unmyelinated nerve fibers of the subepidermal submucosal and perivascular regions (Fig 8 *C*) Collagen fibers found in this layer were identical with that of pars tensa and showed periodic banding in longitudinal section while in cross section, they appeared mostly round Elastic fibers had a cottony appearance with occasional dark filamentous cores (Fig 9 *B*) When they were cut horizontally they *appeared amorphous with a few traces* of fibrils —presumably elastofibrils (Figs 5 and 9 *A*) Periodic bandings in collagen fibers were not present in the form of elastic fibers (Fig 9 *C*) Capillaries



Fig. 3. Electronmicrograph of the epidermis of the sheep's pars flaccida. *C*, stratum corneum; *G*, stratum granulosum; *S*, stratum spinosum; *B*, stratum basale. Abundant glycogen particles are seen in stratum spinosum (arrows).

C
G
S
B
A
5 μ
K
M
B
5 μ

were found mostly near the subepidermal region and to a lesser degree in the submucosal region. Lymph vessels were not clearly recognized by the electron microscopic examination.

Mucous layer

The mucous layer was identical with that of pars tensa except that it was formed occasionally with stratified cells (Fig. 7 B). Goblet cells were found in the cat in association with abundant ciliated cells which could be either cuboidal or squamous (Fig. 10 A and B). They possessed microvilli on their free cell border and could contain secretory granules (Fig. 10 C). The free cell border sometimes showed pinocytotic vesicles. Tonofilaments were not obvious. In a few instances, a terminal nerve seemed to penetrate into the mucous layer. Occasionally, wandering phagocytes were observed along the free cell surface of the mucous layer (Fig. 11).

DISCUSSION

In the previous study of the tympanic membrane pars tensa (Lim, 1968) it seemed apparent that Shrapnell's membrane of the cat and squirrel monkey had a distinct lamina propria. However, due to the tiny size of Shrapnell's membrane in these animals, it became necessary to add the sheep and rabbit to this study because of the larger size of Shrapnell's membrane. The guinea pig was excluded due to the negligible size of pars flaccida.

Fairly accurate orientation of pars flaccida was obtained by a remounting technique which provided the added advantage of permitting the exact measurement of the membrane. Because of the peculiar angulation of pars flaccida, the conventional histologic section of the temporal bone often gave a false impression of this membrane and jeopardized clear interpretation.

In all the specimens examined in this study, it was confirmed that Shrapnell's membrane possessed a lamina propria, which, however, lacked a compact fibrous bundle layer (circular or radial) which was present in pars tensa. The finer fibrils (occasionally rectangular)—the major components of the radial and circular fibrous layer—were not found in this layer. The "only two-layer" concept might have developed from misuse of the term "middle fibrous layer" as synonymous with "lamina propria". "Middle fibrous layer" should only designate the compact fibrous bundle of pars tensa which is described in the author's previous study (Lim, 1968). In live examination it is often thought that pars flaccida looks thinner than pars tensa. However, the pars flaccida of all the animals examined including a

Fig. 4. A. The epidermis of the rabbit pars flaccida. C, stratum corneum; G, stratum granulosum; S, stratum spinosum; B, stratum basale. Arrows indicate the wide intercellular spaces. B. The epidermis of the squirrel monkey pars flaccida. K, keratohyalin granules; M, mitochondria. Large arrows indicate membrane-coating granules (MCG).

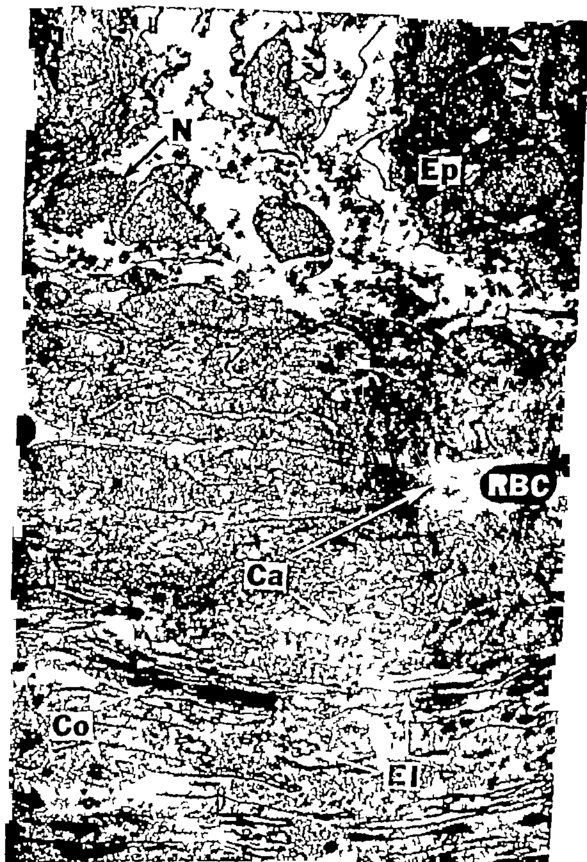


FIG. 3 Electronmicrograph of a port f the pid rml (*Fp*) and l mln propria f the sheep pars flaccida. \ erv f ber C capillaries *RBC*, red blood cell l the l men f a capillary Co collag n fibers; *El* l tl fibers.

FIG. 4. The basal portion of the epidermis of the squirrel monkey, pars flaccida. Arrow indicates light cell. B, basement membrane. B. An electronmicrograph showing abundant nerve fibers in the lamina propria of the squirrel monkey, pars flaccida. Note the nearness to the mucous layer M. F, fibroblast; N, unmyelinated nerve fibers.



Fig 7 (*A*) Th l m propri f the rabbit pars flaccid demo t ll g parall l fibro-bla t (*F*) Arrows i dicat th coll g n fibers. Abu da t l t rcell l am rph u gro nd substances are l ible (*B* A rvey micrograph of the rabbit pars flaccida with the mucous layer n the right d the l mina propria n th l ft



FIG. 8 (*A*) A survey micrograph of subepidermal nerve fiber of the squirrel monkey. Myelinated (M) and unmyelinated (*Um*) nerve fibers are observed. Ca, capillary. (*B*) A longitudinal section of a nerve fiber in the pars flaccida of the squirrel monkey demonstrating local bulging which includes neurogranules and mitochondria (*arrows*). (C) A cross-cut view of nerve of the cat consisting of unmyelinated and myelinated nerve fibers. Mesaxon formations are seen in the unmyelinated nerve fibers. Arrows point to incomplete Schwann cell wrapping. *Ax*, axon; *S*, Schwann cell.



FIG. 7 (*A*) Th lamina propri f the rabbit pars flacc d demonst ti g parall l fibrobl sts (*F*) Arrows indicat th ll g n fibers. Abu da t i t rcell la m rpho grou d substances re isible (*B*) A urv micrograph of the rabbit pars fl ccid with the mucous layer on the right nd th l m propria on the left



FIG. 2. (A) A survey micrograph of subepidermal nerve fiber of the squirrel monkey. Myelinated (M) and unmyelinated (Um) nerve fibers are observed. *Ca*, capillary. (B) A longitudinal section of nerve fiber in the pars flaccida of the squirrel monkey demonstrating local bulging which includes neurogranules and mitochondria (arrows). (C) A cross-cut view of nerve fiber consisting of unmyelinated and myelinated nerve fibers. Mesaxon formation are seen in the unmyelinated nerve fibers. Arrows point to an incomplete Schwann cell wrapping. *Ax*, axon; *S*, Schwann cell.

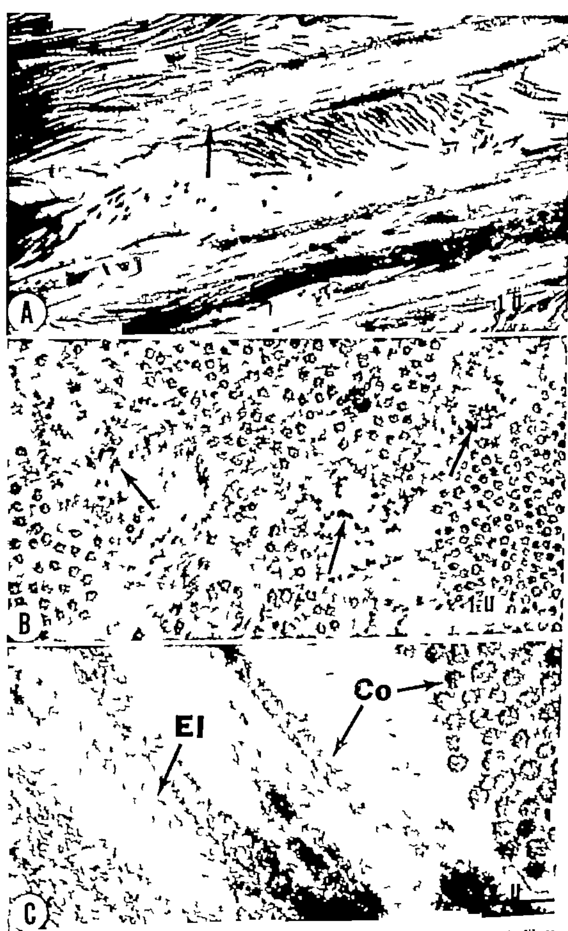


FIG. 9 (*A*) An electronmicrograph demonstrating the fibrillar appearance of elastic fibers in the squirrel monkey (*arrow*). The middle portion of the elastic fibers has a soft amorphous appearance with few elastic fibrils. Regularly banded fibrils are collagen. (*B*) A cross section of elastic and collagen fibers of the squirrel monkey pars flaccida. Arrows indicate dark elastic fibrils. (*C*) High power view of horizontally cut elastic fibers (*El*) of the sheep's pars flaccida compared with collagen fibers (*Co*).

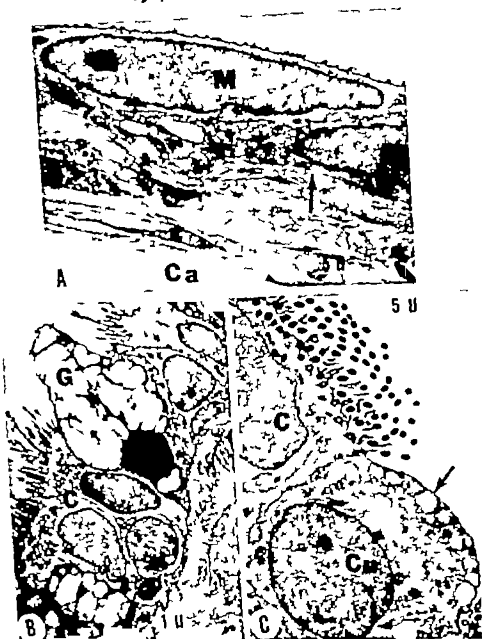
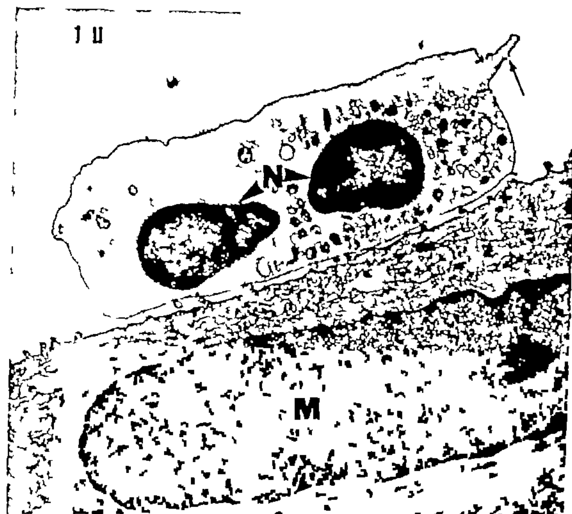


FIG. 10 (A) A simpl squamous type of mucosal pithelial cell (*M*) is seen. The rrow indicates the basement membrane *Ca*, lumen of capillary (*B*) Mucous layer of the cat pars flaccida demonstrates goblet cell (*G*) nd ciliated ell (*C*) (*C*) The mucous layer of the pars flaccida of the cat demonstrates ciliated cell (*C*) nd cuboidal cell (*Cu*) containing secretory granules (*arrow*)



Fi 11 A w ndering ph gocyt l seen on th free surf ce of th mucous lay r of th squirrel m nk y's pars fl ccida. The arrow indi tes pseudopod N nucl u M squa mou cell f th mucous l y

limited number of human specimens, was thicker than pars tensa. This agrees with Araki s (1944) findings in human specimens The arrangement of the fibers of the lamina propria of pars flaccida somewhat resembled that of the stroma of the cornea (Cogan & Kuwabara 1966) The lamina propria of pars flaccida contained more extracellular amorphous ground substance than that of pars tensa, which could account for the relative transparency

The ultrastructure of the nerve endings in this membrane was essentially the same as that of the cutaneous nerve endings (Winkelmann, 1967) however neither the Meissner corpuscle nor the Vater Paccini corpuscle was clearly demonstrated It seemed that all of the unmyelinated nerve fibers were distributed in the subepidermal and submucosal regions, serving as terminal nerve endings. Local dilatations of unit nerve fibers were frequently found along their axes and often contained mitochondria, neurovesicles and neurogranules This finding supported my belief that unmyelinated nerve fibers could serve as nerve terminals. The myelinated nerve became unmyelinated along its course of distribution in the fashion de-

scribed by Engström & Wersäll (1958) The white cells found between the epidermal cells corresponded well with the description of the Merkel cell which conducts a tactile sense (Winkelmann 1967) Shrapnell s original description (1832) of the elasticity of this membrane is well supported by the fact that there were abundant elastic fibers in the lamina propria of pars flaccida. The tubular appearance of the elastofibrils described by Tay lor & Yeager (1966) was not apparent in my specimens. In cross-sectional view the fibrillar cores seemed to be scattered near the margin of the cottony-appearing elastic fibers. No evidence of periodicity in the elastofibrils was found in this material The amorphous ground substance found in the lamina propria of pars flaccida resembled the anhistious ground substance of the basilar membrane of the organ of Corti (Iurato, 1962) This finding may also explain the flaccid nature of this portion of the mem brane

The membrane-coating granules found in the granular cell layer of the epidermis did not occur consistently in my material although many investigators have believed these granules to be closely related to the keratinizing process of the epidermis (Matoltsy & Parakal, 1965 Matoltsy 1966) Frithiof & Wersäll (1965) even suggested that they may be phospholipids.

The mucous layer was similar to that of the middle ear mucosa, and it could accommodate cilia or secretory granules. Secretory cells appeared sometimes as goblet cells with light granules and sometimes as the dark granulated cells found in the middle ear mucosa of the guinea pig (Lim et al 1967 Hussl & Lim, 1968)

ACKNOWLEDGMENT

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ZUSAMMENFASSUNG

Die Feinstruktur der Pars flaccida (Shrapn ll-Membran) des Trommelf lles der Katze des Kanin hens, des Schafes und einer Primatenart (Saimiri sciurea) wurde untersucht. Dabei konnten 3 Gewebsschicht n unterschieden werden ine äussere Epidermisschicht, m mittlere Lamin propria und in innere Schleim hautschicht. Die Epidermis ist aus drei bis vier Lagen verhornender Plattenepi thelzellen ufgebaut. D innere Schl imhautschicht besteht aus einer inzigen Lage von flachen oder kubischen Epithelzellen, die zum Teil Zilien und Sekret granula aufw sen. Die Lamina propria ist aus lockerem Bindegewebe aufgebaut das Fibroblasten Nervenfasern, Kapillaren und reichlich elastische Fasern ver mischt mit unregelmässig angeordneten Kollagenfasern enthält. Die in der Pars

tensa vorhandenen regelmässig angeordneten Kollagenfasern fehlen jedoch. In dem untersuchten Material ist die Dicke der Shrapnell Membran beträchtlich grösser als jene der Pars tensa.

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SYMPTOMATOLOGY UNDER STORM CONDITIONS IN THE NORTH ATLANTIC IN CONTROL SUBJECTS AND IN PERSONS WITH BILATERAL LABYRINTHINE DEFECTS

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Ten labyrinthine defective (L-D) and twenty normal subjects were exposed to extremely severe weather conditions during a sea voyage. The effect of such stress were complicated by a feeling of fear in all of the normal and in some of the L-D subjects. None of the latter manifested typical symptoms of motion sickness whereas all of the normal subject did. The fact that the L-D subject did not become sick suggest that, even in instances where motion sickness symptoms appear to be triggered by anxiety, the vestibular organ plays an essential etiologic role.

The literature regarding increased tolerance to motion sickness in deaf persons dates back to the paper by James (1882). Subsequent studies were conducted by Sjöberg (1931) wherein (1) three young deaf women failed to become sick when hoisted up and down in a crane and (2) four dogs that previously had become sick in the crane were refractory to symptoms when tested again after bilateral labyrinthectomy. Recent attempts have been made to extend Sjöberg's studies by exposing larger groups of vestibular individuals to unusual force environments. In these studies a group of normal males and labyrinthine defectives (L-Ds) were subjected to acrobatics in aircraft (Colehour & Graybiel, 1964; Kennedy & Graybiel, 1962), head movements in the Pensacola Slow Rotation Room (Graybiel et al., 1960), changing linear forces in a counter rotating room (Graybiel & Johnson, 1963) and weightlessness induced by flying Keplerian trajectories (Kellogg et al., 1965). None of the L-D subjects reported symptoms characteristic of motion sickness in any of the above circumstances. On the other hand, typical symptoms of motion sickness were observed in all of the control subjects in one or more of these force environments.

The present study was undertaken partly to determine if L-D subjects could be made sick under severe weather conditions at sea and partly to determine the comparative effects in normal subjects, many of whom were highly resistant to motion sickness under the conditions mentioned above.

Opinions or conclusions contained in this report are those of the authors and do not necessarily reflect the views or the endorsement of the Navy Department. The study was conducted under the sponsorship of the Office of Advanced Research and Technology, National Aeronautics and Space Administration, Order R-93.

PROCEDURE

The Ship

The ship used in this experiment was the MS *Michelon* (French) It was a round bottomed wooden sea going tug and a former U S Army transport It was short (145) narrow (33 beam) light (546 tons) had shallow draft (15 6") and lacked stabilization gear Because of these dimensions, when under way the characteristic motion of this ship was roll However the ship was seaworthy and for several years had been used as a year round ferry and supply ship between North Sydney Nova Scotia and St Pierre/ Miquelon a French possession in the North Atlantic off the coast of New foundland Heavy seas are routine during the winter months, and on some crossings even the ship s crew have reported seasickness.

Subjects and Tests

Twenty controls and ten labyrinthine-defective (L-D) subjects comprised the experimental group All were males in good health The positive function of the vestibular apparatus was assessed by five tests (1) threshold caloric (McLeod & Meek 1962 (2) counterrolling (Miller 1961) (3) a quantitative ataxia test battery (Graybiel & Fregly 1966) (4) Slow Rota tion Room (SRR) performance (Clark & Graybiel 1961) and (5) a Motion Sickness Questionnaire (MSQ) (Hardacre & Kennedy 1963)

1 Threshold caloric

These measurements were obtained by irrigating the tympanic membrane with a stream of water which was controlled for temperature and flow rate. All of the control subjects manifested a clear-cut nystagmic response within 2 0 C of body temperature (34 4 C) and all but two showed nystagmus within 1.5 C (35.5 C) of body temperature In some of the L-D subjects there were instances of a nystagmus response to prolonged irrigation of the ear with water at or below 10 C, but its significance in terms of vestibular function was doubtful in any event it is altogether unlikely that useful semicircular canal function remained in any of these subjects

2 Counterrolling

The counterrolling index (Miller & Graybiel 1963) was normal in the control subjects. Two of the L-D subjects manifested slight (far less than normal) roll The amount of roll was negligible in the remainder

3 Ataxia test

The performance of the controls was far better than that of the L Ds with one exception The one exception was subject Z A who obtained a 50th percentile score on one subtask of the total test (walking eyes

open) This subject, who has much experience in ballet, also responded most like normals to the oculogravic illusion when immersed in water (Graybiel *et al.*, 1967) All L-D scores on *all* other subtests were in the first percentile

4 Slow rotation room

All the subjects were exposed to a standardized procedure the Dial Test (Kennedy & Graybiel, 1965) The subjects were rotated at 7.5 r p.m and if they were symptom free at the conclusion of 100 dial settings, the speed was increased to 10 r p.m. If they were still symptom free after 100 settings, the test was continued at 20 r p m. Some of the control subjects terminated their exposure at one of the three speeds, and three of them completed rotation at 20 r p.m with only very minor symptoms. All the L-Ds executed their tests through 20 r p.m and without symptoms of motion sickness.

M tion sickness questionnaire

The control subject s questionnaires (Hardacre & Kennedy 1963) revealed varied histories of susceptibility to motion sickness. Nine of the control subjects were considered to be highly resistant since their histories showed numerous exposures and almost no symptoms. Two of these nine were senior flight surgeons (B E., M C.) two were retired Navy enlisted men (U P T R.) one was the pilot (C. A) who normally flies airsickness profiles (i.e., aerobatics) in a research aircraft three were regular volunteer laboratory research subjects (D E., V A., J O) and one was on onboard experimenter (K. E.) from earlier Slow Rotation Room studies. The MSQ score of the other eleven control subjects indicated a slightly less than

TABLE 1 *Important vestibular symptoms* used in diagnostic categorization*

Pathognomonic	Major	Minor	Diagnostic terms
Vomiting	Retching		*Vestibular sickness*
	Nausea III or II	Nausea I	Vomiting or
	Inc. saliv III or II	Inc. sali I	Two Major Sym. or
	Pallor III	Pallor II	One Major and
	Cold sweat III	Cold eat II	T Minor Symptoms
	Drowsiness III	Drowsiness III	*Malaise III*
			One Major or
			T Minor or
			One Minor and
			T Other Symptoms
			Malaise I
			Any Subj. Sym. or
			Any Sign usually
			assoc. with subj. ym.
			Malaise II
			All other

I rare instances other symptoms qualify

average history of motion sickness Overall therefore the twenty control subjects could be said to be a group of men with relatively high tolerance to motion

Of the ten L Ds only two reported any past history of motion sickness In each case these were single incidents which occurred in childhood presumably before their loss of labyrinthine function

The results of the findings from these five measures indicated that, while a normal range of vestibular function was manifested in the control group this function was either absent or of no practical significance in the L D group The susceptibility to motion sickness was nil in the L D subjects while the controls as a group were less susceptible than the average

Logistics

The plan was to board the ship in Nova Scotia for the 200 mile trip to the island of St Pierre which would require about 18 hours If the conditions of the trip out were not sufficiently rough then the group planned to remain on the island until a more severe sea state was available for the return crossing

In addition to the assessment of motion sickness symptomatology plans were made to measure postural equilibrium (Fregly & Graybiel 1965) and egocentric visual localization of the horizontal Additionally measurement of biochemical and cardiovascular (orthostatic hypotension) changes were intended but were not done because the experimenters became incapacitated

Motion sickness symptomatology was scored after the method of Graybiel (1964 1966) and the major vestibular symptoms used in this diagnostic categorization are included in Table 1 An observer recorded the signs of motion sickness and the subjects reports of symptoms on a response form When possible, these were administered every 15 minutes during the early portion of the voyage and less frequently later The subjects were also requested to keep diaries and were encouraged to be candid and report anything they may have felt thought, etc

During both crossings all subjects remained mainly in the salon aft or central cabin area amidships (see Fig 1) Both areas were approximately equidistant from the center of gravity and presumably a similar force environment existed in both

The crossing from Nova Scotia to St Pierre was uneventful The sea was calm and the ship s captain claimed that, considering the time of year the trip was one of the smoothest he had experienced Very mild symptoms of motion sickness were reported by only a few men and these subsided rapidly Since the first trip proved unsatisfactory for our purposes, it was decided to await rougher weather for the return

On the afternoon of the fifth day on St Pierre a storm moved by and the group boarded ship that evening Because of the darkness, external

TABLE 2. *Maximum symptomatology during a storm at sea*[*]

Controls		L-Ds	
Subject	Symptoms	Subject	Symptoms
S. A.	Emesis	D. O.	Drowsiness (see text)
W. H.	Emesis	G. R.	Drowsiness
M. C.	Emesis	G. A.	Drowsiness
D. A.	Emesis	H. A.	Throat constriction
R. E.	Emesis		slight nausea (see text)
L. P.	Emesis	J. O.	Drowsiness
S. T.	Emesis	L. A.	Salivation— bile eati g
R. I.	Emesis	M. A.	General discomfort
T. R.	Emesis	P. C.	Drowsiness
A. L.	Emesis	S. T.	Gas on the stomach
T. D.	Emesis	Z. A.	Drowsiness
C. A.	Emesis		
K. F.	Emesis		
T. B.	Emesis		
P. O.	Emesis		
O. A.	Malaise III		
J. O.	Malaise III		
D. O.	Malaise III		
A. A.	Malaise III		
D. E.	Malaise II		

Control subjects ranked by onset of sickness, L-D subjects listed alphabetically

Visual reference aboard ship was minimal. The ship cleared the harbor at 2100 hours. The sea condition was very rough: waves estimated at 40 feet, and these produced an estimated roll displacement of 40+ degrees. Winds of 40 knots (gusts to 80 knots) were encountered for most of the first eight hours under way, after which the weather subsided. Acceleration recordings showed a seend of >2 G and roll rate of >10°/sec. A further testimony to the condition of the sea is the fact that two larger commercial ships sailing through the storm foundered and broke up. The return trip lasted 28 hours, which was half again as long as the trip out.

RESULTS

Table 2 shows the maximum symptomatology experienced by the control group and the L-D subjects. The control group is ranked by onset of emesis with the earliest ranked first. The five subjects who did not vomit are ranked by their degree of sickness and how soon maximum symptoms appeared. The first subject to vomit did so almost immediately after the ship hit rough water, and others followed shortly after. The 15 men who

[*] A recent (1967 National Geographic) survey suggests that weather conditions in this area cause it to have the highest incidence of lost ships in the world.

vomited all had their first episode within two to three hours under way and many continued to vomit throughout the night As the sea condition became less violent vomiting episodes were less frequent by the time the ship docked after 28 hours at sea most of the control subjects (but not all) had fully recovered.

The L-D subjects are listed alphabetically in Table 2 along with their chief complaints One of the ten L D subjects reported "gas on the stomach" and another constriction in the throat The latter also recorded slight nausea on his response form but when questioned later he claimed it was "cerebral and not gastrointestinal" All ten mentioned general discomfort due to the physical environment six reported drowsiness" probably due to the late hour but none of them slept Fear was also mentioned in their diaries None of these L-D subjects however manifested symptoms which were considered to be typical of motion sickness

The control subjects ranking were compared with an experimenter's ratings of their performance in the SRR and of their responses on the MSQ The rating scale which was employed classified the subjects as (1) far more susceptible than average (no subject fell in this group for the MSQ and only one for the SRR test) (2) more than average (3) average (4) less than average and (5) far less susceptible than average Pearson product moment correlation coefficients for these variables appear in Table 3 All are statistically significant[1]

DISCUSSION

The results of this experiments appear to be clear cut None of the L-D subjects exhibited characteristic symptoms of seasickness whereas three fourths of the controls vomited, and the rest suffered Malaise III or II (cf Table 1)

The high correlations which were obtained between the SRR and MSQ pretests of susceptibility and the time or degree of seasickness point out the existence of a general factor of susceptibility to motion sickness and demonstrate the need for adequate evaluation and selection of subjects prior to their use in motion sickness research For example, in the studies of drug effectiveness or of the influence of temperature or of odors, etc in various force environments (e g., air sea, zero gravity) an adequate preliminary assessment of the experimental population would be critical to the research design This is particularly important when the sample size is small and a subject is exposed more than once (e g in order to serve as his own control)

With regard to the psychogenic cause of motion sickness all of the L-D subjects reported discomfort from the physical environment and some

[1] The range of susceptibilities in this population is restricted since nearly all of the control subjects were of less than average susceptibility A more heterogeneous population would be likely to provide higher correlations.

reported that they were afraid. On the other hand, many of the control subjects who expressed fear did not begin to record these fears in their diaries until after their seasickness symptom subsided. Yet the L-D subjects were extremely anxious throughout the first evening and none vomited. Indeed they would not (or could not) go to sleep, but secured themselves t chairs in the salon and tried to play cards. It is felt that were it possible for motion sickness symptom to be precipitated by fear such as some experienced, then they surely would have become sick. However the fact that they did not become sick suggests, if it does not prove that, even in other instances where motion ickness symptoms appear to be triggered by anxiety the vestibular organs play an es ential etiological role. Stated differently anxiety may modulate the severity of motion sickness symptoms, but inasmuch as the relative contribution of their influence upon a control subject's performance is unknown, in the absence of verifiable vegetative reactions in the L D subjects it is suggested that the vestibular stimulu was the maj r contributing component.

In summary it is concluded that (1) the presence of vestibular function is a necessary requirement for the experience of m ti n sickness symptoms under seagoing conditions and (2) susceptibility a observed in a very rough sea condition is highly correlated with susceptibility as assessed by a laboratory technique for producing canal sickness and with past history of motion sickness.

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ZUSAMMENFASSUNG

Zehn Labyrinthdefekte (L-D) d zwanzig orm l Versuchspersonen wurden extremen Schlechtw tterverhaltnissen uf l er Seereise usgesetzt Die Wirkungen dieses Stresses waren weiter kompliziert d rch A gstgefühl fü alle normalen und fur inige L-D-Versuchsperso en keine der letzteren zeigte typisch Seekrankheits ymptom während lle n rmalen erkrankten Der Umst d dass die L-D-Versuchspersonen nicht krank wurden legt n he dass selbst in Fällen wo Seekrankhe tssymptome durch Angst ausgelöst werde die vestibulären Organ eine wichtige ätiologische Rolle spi len

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ELECTRON MICROSCOPIC STUDY OF SEMICIRCULAR CANAL ORGANS AND OTOLITH ORGANS OF SQUIRREL MONKEYS AFTER ADMINISTRATION OF STREPTOMYCIN SULFATE[1,2]

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Pathological findings in the ultrastructure of the semicircular canal and otolith organs of squirrel monkeys after administration of streptomycin sulfate are described. The monkeys were sacrificed at predetermined points in the suppression of their vestibular function as shown by the caloric threshold value and the cristae and maculae examined by electron microscopy. Initial ultrastructural pathology of vestibular apparatus was observed. At all points of vestibular suppression, the most striking feature was that no significant pathology of ultrastructure was seen in the h l ll f the saccular maculae but was observed in the sensory epithelium of the utricular macula and crista. The ototoxic mechanism of streptomycin to the vestibular neuroepithelium was discussed from the morphophysiological point of view.

There have been numerous published reports during the last 20 years on the toxic effects of streptomycin, the most common effect reported being the eighth nerve damage seen in man and animals.

The site of the ototoxic action of streptomycin has been studied pathologically by Rüedi *et al.* (1940), Berg (1951), Christensen *et al.* (1951), Hawkins & Lurie (1952), Lurie (195), Schuknecht (1957), McGee & Oleszewski (1962) and others, all of whom have stated that the lesions are definitely in the end organs in both the vestibular and cochlear systems. On the other hand, Cherkasov (1964) reported that the pathological changes were in the cells of the vestibular ganglia, and Winston *et al.* (1948 and

[1] This research was conducted under the sponsorship of the Office of Advanced Research and Technology, National Aeronautics and Space Administration. Opinions or conclusions contained in this paper are those of the author and do not necessarily reflect the views or endorsement of the Navy Department.

[2] The experiments reported herein were conducted according to the principles enunciated in "Guide for Laboratory Animal Facilities and Care" prepared by the Committee on the Guide for Laboratory Animal Resources, National Academy of Sciences, National Research Council.

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TABLE 1 *Summarized data obtained from six streptomycinized squirrel monkeys at the time of sacrifice*

		Daily dosage (mg/kg)	Total dosage (mg/kg)	Duration (injections) (days)	Sacrificed (days) after last injection	Caloric threshold at sacrifice time (°C)	Dynamic equilibrium values at sacrifice time (r.p.m.)
Early suppressive stage	C81	200	1600	10	3	31.0	—
	C80	200	2200	11	2	27.1	850
	C83	200	3800	21	7	25.6	200
	C84	200	3100	26	2	21.8	0
Advanced suppressive stage	D05	200	2000	11	7	6.0	0
	C85	200	3000	18	11	2.0	200

specimen was dissected out and remounted in the proper directi n For orientation and light microscopic cell population counting one micron section stained by buffered toluidin blue solution was used. Thin sections cut at 600 Å to 1000 Å were prepared with LKB ultratome The preparations were examined in a Philips EM 200 operated at 60 KV

RESULTS

A relatively large daily dose of streptomycin was applied in order to obtain sure and quick suppression of vestibular function In almost all cases, only a few injections of the 200 mg/kg of streptomycin sulfate were needed to cause an initial decline in the caloric threshold value As shown in Fig 1 this value decreased slowly at first then dropped suddenly to the point of maximum suppression All animals in the present experiment were killed within 30 days after the first injection.

In general pathological observations, microscopic examinations of sections of tissues and organs from each experimental animal showed no recogniz able abnormalities except for para ites and microfilariasis in a few cases

To fill the gap between the electron microscopic specimens and an o dinary 20 or 25 microns serial section of the temporal bone, a one-micron section of an epon embedded pecimen was applied The evaluation of hair cell damage was first carried out by using one micron sections. Some degree of hair cell damage wa seen in all cristae from the animals in early and ad anced stages of vestibular suppression. Pathology of the sensory epithelium f the cristae correlated well with the time of sacrifice The crista from a very early stage of vestibular suppression appeared almost n rmal (Fig. 2 A) whil the crista of an advanced suppressive stage exhibited obvious hair cell loss (Fig 2 B) All six saccular maculae were nearly

1949) that they were in the central vestibular apparatus Dosage of the drug and the time of sacrifice might cause the different pathology Some systematic comparison with light microscopic procedures of the cristae and maculae of given streptomycin animals has been reported Igarashi *et al* (1966) recognized that a well-designed procedure of streptomycin administration caused pathological changes in the maculae different from those in the cristae.

Although Wersall & Hawkins (1962) demonstrated a relatively selective effect on the sensory cells in the vestibular apparatus and Duvall & Wersäll (1964) reported the early stage of damage caused by streptomycin to be in the sensory cells of inner ear there are still no electron microscopic studies which compare systematically the ultrastructure of the semicircular canal organs with that of otolith organs in correlation with vestibular functions

The present paper compares the ultrastructures of the semicircular canal organs and otolith organs during early and advanced suppression of vestibular functions after administration of streptomycin sulfate on squirrel monkeys

MATERIALS AND METHODS

Six healthy squirrel monkeys (*Saimiri sciureus*) weighing between 500 and 600 g were selected on the basis of normal vestibular functions as tested by the threshold cold caloric test (McLeod & Meek 1962) and by the dynamic equilibrium test for monkeys (Igarashi, 1968)

All six monkeys received 200 mg/kg of streptomycin sulfate per day intramuscularly Administration was continued until the monkeys showed a certain degree of vestibular suppression as indicated by the caloric threshold

Two different stages of vestibular function suppression were selected as the criteria to decide the time the animals were sacrificed Six monkeys were grouped as follows The early suppressive stage Four monkeys were sacrificed when their caloric threshold values declined in decrements of 2 C to 10 C from their pre-experimental valve The advanced suppressive stage The remaining two monkeys were sacrificed when their caloric threshold values indicated complete suppression of vestibular function

Data of drug dosage vestibular function tests, and the sacrifice time from six animals are summarized in Table 1

Under general anesthesia with intraperitoneal pentobarbital the labyrinth of the monkey was opened after routine stapedectomy by using an operating microscope and the entire vestibular organs were fixed *in situ* with cold Millonig s solution (Millonig, 1962) The cristae ampullaris of the lateral and superior semicircular canals maculae utriculi and sacculi, and a part of stria vascularis were carefully taken out as a whole Electron microscopic specimens were embedded in Epon 812 (Luft 1961) Each

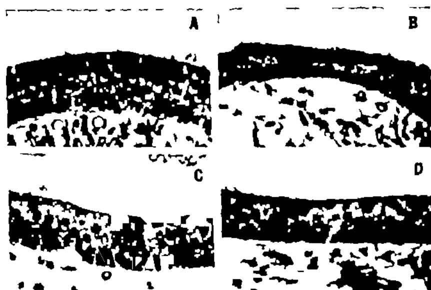


FIG. 2 (A) Photomicrograph d monstrat g lmost intact ppearance i the superior canal crista f om the ea of squirrel monkey (C31) which w sacrificed t the ea ly stage of estibula ppres ion. 320 (B) View of the severely dam ged sensory epithelium of the horizont l canal crista from imal (DO5) which was killed at ad anced suppressiv tage. 320 (C) Phot micrograph exhibiti g i tact macula sacculi from an animal (C32) of ad nced suppressi stage 320 (D) Phot micrograph show ing moderate loss of hai cell in the macula triculi from monkey (DO4) i d nced stage f ppressi 320.

plasmic protrusions of the apical part of the hair cells. However in the vestibular neuroepithelium of the animal from this stage no obvious mem branous change was observed in the endolymphatic surface of the hair cells type 2

Transfigurations of the nucleus of the hair cells type 1 were the next ultrastructural pathology observed Uneven distribution of chromatin in the nucleus, irregular cont urs of the nucleus, occasionally forming deep clefts, lamellar formations and eventually scattered chromatin in the cytoplasma were seen in the utricular maculae and crista (Fig. 6)

The findings of my inquiries int the pathology of the vestibular organ f m nkeys of the early suppressive stage can be summarized thus (1) variegated and tive ultrastructural changes of the organellae in the hair cells type 1 of the macula utriculi in the same way as in the crista (Fig 7) (2) no significant ultrastructural pathology in the macula sacculi and (3) no manifest changes of the organellae in the hair cells type 2 of all vestibul r neuroepithelium.

2 *Advan ed suppr ssive group*

Severe pathological changes were observed in the cristae of all cases in this group The sensory epithelium of the horizontal canal crista exhibited

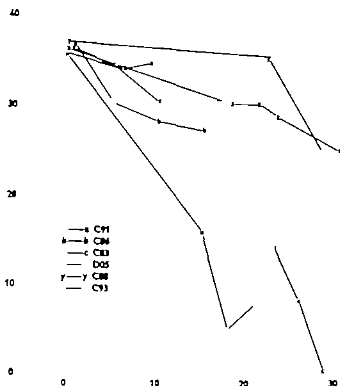


Fig. 1 Graph showing the tim course of the caloric threshold of ix squirrel m nk ys afte strept mycin administrati n. The abscissa rep esents days after first injecti n, and the ordinat i dicates the caloric threshold (C)

normal in appearance, as exemplified in Fig 2 C However the sensory epithelium of the utricular maculae showed moderate pathology in one case (Fig 2 D) but four other utricular neuroepithelia demonstrated extremely light changes in light microscopic level

Electron Microscopic Observations

1 *Early suppressive group*

Vacuolar formations in the apical area of hair cells type 1 in the sensory epithelium of the crista and macula utriculi was one of the significant initial ultrastructural changes caused by streptomycin sulfate (Fig 3) This was followed by the endolymphatic membranous changes which usually occurred first at the non-cuticular area of the hair cells.

Changes in mitochondria were also common findings in the hair cells type 1 of the cristae and utricular maculae from the monkeys of the early suppressive stage There were two types of mitochondrial transfigurations which were observed in the supranuclear part of the hair cells from the monkeys of this stage (*a*) swollen and electron light mitochondria (Fig 4) and (*b*) irregular and electron-opaque mitochondria (Fig 5) Often the mitochondrial changes were observed prior to the changes of the surface area of the hair cells.

Further development of the membranous changes was observed as cyto-

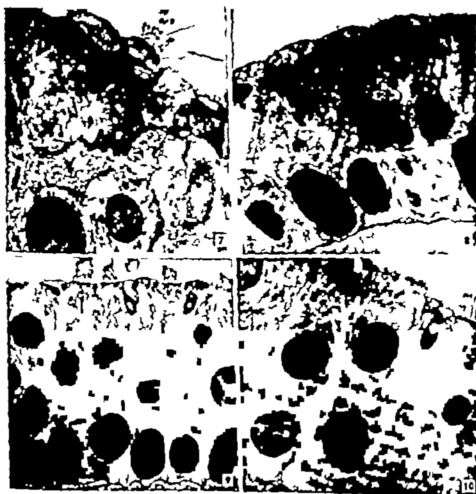


Fig. 7. Sensory epithelium of the uperior canal crista from the monkey (C84) of ea ly ppressan stage. Arrow ndicates membranous pathology t the surface area f hair cells type 1. Also mitochondrial changes are observed i the cytoplasma f hair cell type 1. 2300.

Fig. 8. Sensory epithel um of the horizontal canal crist from a monkey (DO5) of ad nced ppresan stag. Not the disappearance of both hai cell types 1 nd 2. 1710.

Fig. 9. Sensory epithelium of the macul utriculi from monkey (DO5) f d nced uppresal stage. Disappearance of considerable number of hai cell type 1 was observed. 1710.

Fig. 10. Sensory epithelium of the macula sacculi from monkey (DO3) of advanced suppresal stage. N significant pathology in hair cells, both types 1 and 2 are seen. 1710.

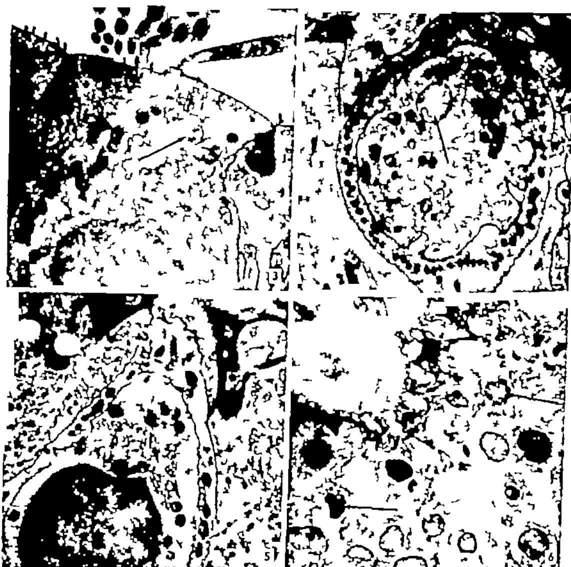


Fig 3 Vesicular f rm tion (*arrow*) in th pical arc f th hai cell t pe 1 I the sensory pith lium of the supe lo canal erista f m an nimal (C93) which received 3800 mg kg f tı pt my in. 9300

F a. 4 A sw ll n mitochondri n (*arr w*) I cyt pla m f hai cell t pe 1 I the upe ior can l cri t (C88) This l rg type of mitocho dria i mm in the nerve challee f the no m l m nkey but i not present n the cyt pla ma f n rmal hair cells. × 9300

Fig. 5 Type 1 hai ll in the h riz ntal ca l ri ta of a trept m int icated monkey (C86) F rmati n of d k irregul granules in the m toch ndri manifest. 9300

Fig. 6 Lower magnificati n of lightly bliq secti ed nsory epith li m f th macula utriculi from m nkey (C93) of th ea ly ppres i t g Arrow i dicat deformed nuclei of hai cell typ 1 with u ven di t ibuti of hrom ti d hange of contour × 1430

At the cellular level

(*a*) Hair cells type 1
(*b*) Hair cells type 2

At the level of the cell organellae

(*a*) Vacuolar formation in the apical area of hair cells.
(*b*) Mitochondrial transfigurati ns in hair cells.
(*c*) Rupture of the non-cuticular surface of hair cells.
(*d*) Swelling of hairs.
(*e*) Apical protrusions of the supranuclear cytoplasma
(*f*) Transfigurations of nucleus in several stages.
(*g*) Diversity in the process of hair cell destructi n
(*h*) Transformation of nerve chalice
(*i*) Disappearance of hair cells.
(*j*) Mitochondrial pathology in nerve endings on I nerve fiber

DISCUSSION

The original purpose of the present paper was (1) to clarify the dif ferent sensitivity of each vestibular end apparatus to streptomycin toxicity and (2) to establish the order of streptomycin damage to the cell organellae of the sensory epithelium of vestibular end organs. Intramuscular ad ministration of streptomycin produced a relatively low concentration of the drug in th endolymph, i.e the maximum concentration of streptomycin in the inner ear amounted to approximately one per cent of the maximum blood level (Voldrich, 1965) This low concentration of streptomycin in the endolymph at the early stage of intoxication caused relatively light patho- logy in the sensory epithelium of the vestibular apparatus in comparison with the severe pathology which was caused by local application of the drug (Spoendlin, 1967) However after the accumulative effect of drug was completed in the end lymph, a severe pathology was also expected in the vestibular neuroepithelium of intramuscularly injected cases.

The present experiment confirmed that the initial toxic mechanism of streptomy in to the vestibular sensory cells occurred in the following order mitochondrial changes—endolymphatic membranous changes—nuclear changes. This is upported by the proposed mechani m of streptomycin to the bacterial cells, i.e (1) damages to the enzymic system in th TCA cycle electron transport ystem and oxidative phosphorylation, (2) damage to th cyt plasmic membrane, especially the alteration of the permeability of the cell membrane and (3) the inhibition of protein synthesis and ribo- som function (Gale 1963) All the enzymes and coenzymes necessary for th energy-generating mechanism of cell metabolism are now known to be located in the membrane of mitochondria. Ther fore, th changes of the mitochondria suggested an impairment of cell metabolism, and th changes of cytoplasmic membrane and nucleus indicated damage or inhibition of

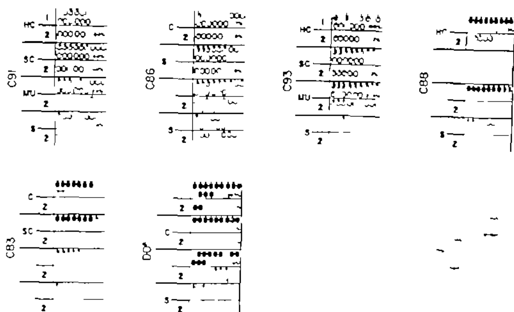


Fig 11 Ultrastructural pathology of vestibular end organs from monkeys after streptomycin administration Blackened area of the circle indicates the estimated cell loss by pathology by combining electron microscopic findings with light microscopic data Percentage represents the estimated mean value of the damage in each sensory epithelium (number of circles does not show the exact number of cells which were checked) *HC* Horizontal canal crista *SC* superior canal crista *MU* macula utriculi *MS* macula sacculi; *1* hair cell type 1 hair cell type 2.

disappearance of both type 1 and type 2 hair cells extending from the summit area to the slope area (Fig 8) The disappearance of a considerable number of hair cells type 1 in the macula utriculi was also observed in the same animal (Fig 9) while there was little manifest ultrastructure pathology in the macula sacculi (Fig 10) The characteristic findings in the vestibular neuroepithelial pathology of the advanced suppressive stage were (1) severe damage of the crista epithelia extending to the disappearance of hair cells type 1 and sometimes type 2 (2) loss of hair cells type 1 in the utricular macula and (3) no apparent pathology in the ultrastructure of the sensory epithelium of the saccular macula except minor changes in the mitochondria in hair cells type 1

The degree of ultrastructural pathology in the vestibular end organs from the monkeys which received the same daily dose of streptomycin, but were sacrificed at different stages of vestibular suppression are summarized in Fig 11

From the point of view of ultrastructural pathology the damage caused by streptomycin sulfate was demonstrated to occur in the following order

At the organic level

(*a*) Cristae
(*b*) Macula utricula
(*c*) Macula sacculi

At the cellular level

(*a*) Hair cells type 1

(*b*) Hair cells type 2.

At the level of the cell organellae

(*a*) Vacuolar formation in the apical area of hair cells

(*b*) Mitochondrial transfigurations in hair cells.

(*c*) Rupture of the non-cuticular surface of hair cells

(*d*) Swelling of hairs.

(*e*) Apical protrusions of the supranuclear cytoplasma

(*f*) Transfigurations of nucleus in several stages.

(*g*) Diversity in the process of hair cell destruction

(*h*) Transformation of nerve challce

(*i*) Disappearance of hair cells.

(*j*) Mitochondrial pathology in nerve endings and nerve fiber

DISCUSSION

The original purpose of the present paper was (1) to clarify the different sensitivity of each vestibular end apparatus to streptomycin toxicity and (2) to establish the order of streptomycin damage to the cell organellae of the sensory epithelium of vestibular end organs. Intramuscular administration of streptomycin produced a relatively low concentration of the drug in the endolymph, i.e. the maximum concentration of streptomycin in the inner ear amounted to approximately one per cent of the maximum blood level (Voldrich, 1965) This low concentration of streptomycin in the endolymph at the early stage of intoxication caused relatively light pathology in the sensory epithelium of the vestibular apparatus in comparison with the severe pathology which was caused by local application of the drug (Spoendlin, 1967) However after the accumulative effect of drug was completed in the endolymph, a severe pathology was also expected in the vestibular neuroepithelium of intramuscularly injected cases.

The present experiment confirmed that the initial toxic mechanism of streptomycin to the vestibular sensory cells occurred in the following order mitochondrial changes—end lymphatic membranous changes—nuclear changes. This is supported by the proposed mechanism of streptomycin to the bacterial cells, i.e (1) damages to the enzymic system in the TCA cycle electron transport system and oxidative phosphorylation (2) damage to the cytoplasmic membrane especially the alteration of the permeability of the cell membrane, and (3) the inhibition of protein synthesis and ribosome function (Gale 1963) All the enzymes and coenzymes necessary for the energy-generating mechanism of cell metabolism are now known to be located in the membrane of mitochondria. Therefore the changes of the mitochondria suggested an impairment of cell metabolism, and the changes of cytoplasmic membrane and nucleus indicated damage or inhibition of

protein synthesis of the cell though the bacterial mechanism possesses some features different from that of the mamalian sensory cells

To explain the different vulnerability of the cristae and maculae to streptomycin sulfate more exactly the different sensibility of the utricular canal system and saccular system it must be necessary to consider the following points (1) morphophysiological relationship and difference between utriculo-canal system and saccular system (2) streptomycin concentration in the endolymphatic system

From the morphological point of view it is quite possible that the streptomycin concentration in the saccular endolymph is different from that in the utriculo-canal endolymph Between the utriculus and sacculus the ductus utriculo-saccularis is the aqueduct and the utriculo-endolymphatic valve regulates the endolymphatic flow from the side of the utricular sac to the side of the utricular duct. The saccular system is thought to be a rather separated closed system with two small ducts one to the cochlear system (Ductus reuniens) the other to the utricular system (Ductus utriculo-saccularis which is connected with Ductus endolymphaticus) Igarashi (1965) confirmed this arrangement of the saccular system in his experiment with saccular destruction on squirrel monkeys

Furthermore, the ultrastructure of the epithelial linings of the ampullae i e the transitional cell layer planum semilunatum, and dark cell layer demonstrated some features which are suggestive of a secretory and reabsorptive process (Dohlman 1964 1965 Kimura *et al* 1964) In the cochlear system, the stria vascularis with spiral ligament because of the structural configurations and high metabolic activity has been regarded by many investigators as the area of secretion and absorption of endolymph (Smith 1957 Rodriguez Echandia & Burgos, 1965 Johnson & Spoendlin 1966 and others)

The presence of secretory and absorptive cell layers in the utriculo-canal and cochlear system and the nonexistence of these particular epithelia in the saccular system should be considered as an important factor in causing the different pathology between the utriculo-canal and the saccular system The entrance of streptomycin into the inner ear from the blood was presumed to be through secretory epithelia into endolymph under the conditions of selective passage. In the utriculo-canal system the planum semilunatum secretes endolymph and the dark cells absorbs it and thus both cells cooperate in maintaining a certain level of drug concentration after drug administration In the cochlea, the endolymph was actively filtered through Reissner's membrane from the perilymph excess fluid and waste products being absorbed by the stria vascularis (Ormerod 1960) Thus, sensory epithelia of the utriculo-canal and the cochlear system were exposed to the danger of drug infiltration from the early stage of intoxication while the sensory epithelium of the saccular system might not be exposed to the secretory and absorptive activity of streptomycin contained endolymph in the stage of acute intoxication

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ZUSAMMENFASSUNG

Die ultrastrukturelle pathologischen Befunde der semizirkularen Kanalorgane und der Otolithorgan von sechs T tenkopfäffchen na h Streptomycinverabreichung werden beschrieben Di Affen wurden getötet zu vorbestimmten Zeiten, die von dem Funktionszustand der estibularen Organe abhä gen welcher durch kalorische Schwelle bestimmt wurde Cristae und Maculae wurden elektronenmikroskopisch untersucht. In llen Stadien der vestibularen Funktionsverminderungen war das auffallendste Merkmal, d ss k l e bedeutende ultrastrukturelle Pathologie in den Haarzellen der saccularen Maculae vo lag, währe d die sensorischen Epithelien der utricularen M culae mehr oder weniger pathologische Veränderungen ufwiesen. Die anfängliche ultrastrukturelle Pathologi der vestibularen sensorischen Epithelien inf lge Streptomyci wurde besprochen Die wichtige Rolle der sekret rischen und absorptiven Epithell n im ampullo-utricularen Gebi t wird gez igt und als Erklärung der Befund herangez gen

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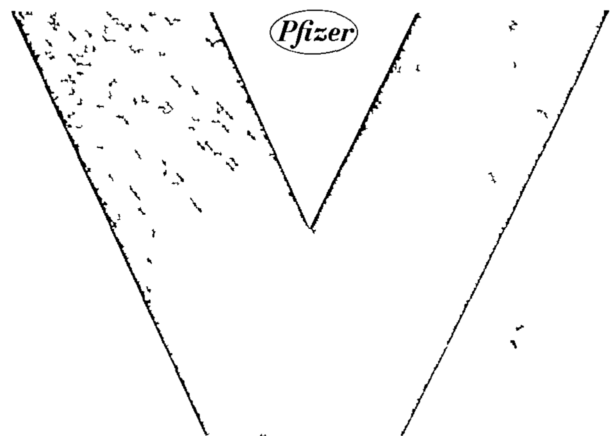
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